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## RESULTS OF PARTIAL GASTRECTOMY FOR BLEEDING DUODENAL, GASTRIC, AND GASTROJEJUNAL ULCER \*

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*Types of Bleeding Peptic Ulcer.*—Two principal types of gross hemorrhage occur from peptic ulcer: the chronic, which is associated with hematemesis or melena but does not give rise to severe symptoms of loss of blood even though the bleeding may be considerable, and the acute massive, which is associated with marked sweating, pallor, weakness, prostration, fast thready pulse, and circulatory collapse. Recognition of these types is important not only in order to understand the mortality from bleeding but also in order to institute proper treatment.

*Mortality Rate from Hemorrhagic Peptic Ulcer.*—A study of the literature on hemorrhagic peptic ulcer indicates that between 25 and 35 per cent of patients who had peptic ulcer have had episodes of bleeding. When all the cases of peptic ulcer are considered without regard to the type of hemorrhage or to treatment, the mortality rate seems low, probably from 1 to 3 per cent in cases of gastric and duodenal ulcer, but two to three times higher in cases of gastrojejunal ulceration. However, when the massive type of hemorrhage is studied to determine the mortality rate in this type of case, an entirely different picture is evident, as Allen and Benedict,<sup>3</sup> Blackford and Cole,<sup>6</sup> and Blackford and Williams<sup>7</sup> have emphasized. These observers stated that approximately 50 per cent of patients age 45 or more, who bled from ulcers have had the massive type of hemorrhage, and that 33 per cent of such patients if treated expectantly will die from hemorrhage.

*Treatment of Bleeding Peptic Ulcer.*—*Acute Massive Hemorrhage:* In acute massive hemorrhage from peptic ulcer, cessation of bleeding occurs

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with rest, blood transfusion, and proper diet in most cases when the patients are less than age 45, and in about 70 per cent of cases when the patients are more than age 45. Obviously, the results from conservative measures cannot be improved greatly by surgical intervention in the younger age-group. The presence of arteriosclerosis, and the difficulty of contraction and thrombosis in an eroded, thickened artery are the probable explanation for the continuation of the bleeding and the higher mortality rate among patients in the older age-groups. The problem which presents itself is how to recognize the 70 per cent of patients who will recover from the effects of the massive hemorrhage under medical treatment, some of whom might die as a result of surgical interference, and conversely, to recognize which of the 30 per cent who die under medical treatment could be saved by surgical treatment. There is a difference of opinion on both phases of the problem between surgeons and internists. One reason for this is due to the fact that an insufficient number of patients who have acute massive hemorrhages from peptic ulcer, have been treated surgically to prove any reduction of mortality in the older age-group by the surgical treatment. Furthermore, there is a great difference between emergency operations performed at the time of, or shortly after, the hemorrhage occurs and several days later, when a nephrotic condition with retention of nitrogen and frequently edema greatly increase the operative risk. Finsterer,<sup>13</sup> however, reported that he has operated upon 78 patients within 48 hours of the onset of massive hemorrhage. Only four died, a mortality rate of 5.1 per cent. Three deaths (a mortality rate of 4.2 per cent) occurred in the 71 cases in which partial gastric resection was performed, and one death in the seven cases in which gastro-enterostomy was done. Of 74 patients treated later, that is, more than 48 hours after onset of massive hemorrhage, 22 died (a mortality rate of 29.7 per cent). Eleven of the patients who were treated early were between ages 60 and 80. Such a large series has not been reported by any other surgeon, nor have such low figures for operative mortality been obtained. This probably is due in part to the small number of cases in the other series.

Gordon-Taylor<sup>16, 17</sup> recently reported a mortality rate of 19 per cent (32 cases, with six deaths) in cases of massive hemorrhage in which operation was performed early. Thus, while the value of surgical treatment in acute massive hemorrhage is not proved beyond doubt, on theoretic grounds, at least, eroded arteries in the bases of such ulcers must be attacked surgically among the older patients to reduce the mortality. Finsterer's experience emphasizes the seriousness of a few days' delay in operating upon such patients. The corollary to this seems to be that patients more than age 45 who have massive hemorrhage should be operated upon immediately, that is within 24 to 36 hours after onset of the hemorrhage, or should not be operated upon until they have recovered entirely from the effects of the hemorrhage.

The results of the treatment of acute massive hemorrhage from peptic ulcer at the Mayo Clinic are not entirely clear, largely because of failure in



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the past to classify in a separate group the cases of acute massive gastric or duodenal hemorrhage. For the most part, in the past, medical treatment has been employed for such lesions and surgical treatment has been postponed until the patient has recovered fully. When surgical attack has been utilized, it usually has been carried out only after medical measures have failed to control the bleeding. The operative results, in general, are in accord with the findings of others, namely, that operative treatment in the terminal stages has proved relatively hopeless and the more favorable results have been obtained in the few cases in which operation was performed soon after the onset of the hemorrhage.

*Chronic Hemorrhage.*—Treatment of chronic hemorrhage from peptic ulcer is an entirely different problem. Here, interest lies in prophylaxis

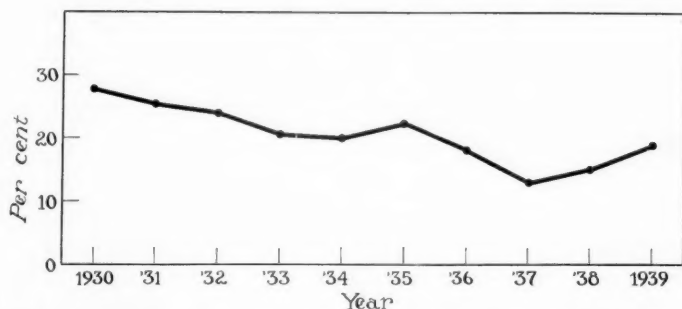


CHART 1.—Percentage of patients who had duodenal ulcer treated surgically.

against further hemorrhage and relief from intractable symptoms of ulcer. The surgical procedures employed and their indications are of great importance (Chart 1). In cases of bleeding duodenal ulcer, it was formerly thought that gastro-enterostomy afforded protection against further serious bleeding. However, 227 of a series of 336 patients, who had undergone gastro-enterostomy for bleeding duodenal ulcer at the Mayo Clinic,<sup>5</sup> were traced for seven or eight years after operation. Sixty-six (23.8 per cent) had bled subsequently. In order to evaluate the effectiveness of partial gastrectomy for bleeding peptic ulcers, a study was undertaken of a group of patients operated upon during a five-year period (1932–1936, inclusive).

### STUDY OF CASES OF BLEEDING PEPTIC ULCER, IN WHICH PARTIAL GASTRECTOMY WAS PERFORMED AT THE MAYO CLINIC

All the partial gastric resections for bleeding peptic ulcer at the Mayo Clinic, from 1932 to 1936, inclusive, were chosen for study. This period followed the return of one of us (Walters<sup>28</sup>) from Europe; in various European clinics extensive gastric resections had been observed for peptic ulcer.

*Duodenal Ulcer.*—Partial gastrectomy was performed for duodenal ulcer

in 99 cases, from 1932 to 1936, inclusive; in 42 (42.4 per cent) of these, it was performed for hemorrhagic duodenal ulcer. In the year 1940, at the Mayo Clinic, 138 partial gastrectomies were performed for duodenal ulcer, of which 73 (52.9 per cent) were for hemorrhagic duodenal ulcer (Table I). On the basis of approximately 25 per cent of duodenal ulcers being associated with bleeding, in about 2.5 per cent of cases of bleeding duodenal ulcers, and 1 per cent of cases of duodenal ulcers without history of gross hemorrhage, partial gastrectomy was performed, from 1932 to 1936, inclusive. In 1940, partial gastrectomy was performed at the Mayo Clinic in about 13 per cent of the cases of bleeding duodenal ulcers, and in about 4 per cent of those of nonhemorrhagic duodenal ulcers (Chart 2).

TABLE I

INCIDENCE OF HEMORRHAGE AND OPERATIVE MORTALITY RATE AMONG PATIENTS TREATED FOR PEPTIC ULCER BY PARTIAL GASTRECTOMY AT THE MAYO CLINIC, 1932-1936, INCLUSIVE, AND 1940

Lesion	Partial Gastrectomy, 1932-1936, Inclusive				Partial Gastrectomy, 1940		
	For Hemorrhagic Lesions				For Hemorrhagic Lesions*		
	Total Cases	Cases	Per Cent	Operative Mortality Rate, Per Cent	Total Cases	Cases	Per Cent
Duodenal ulcer	99	42	42.4	7.1	138	73	52.9
Gastric ulcer	114	25	21.9	12	82	17	20.7
Duodenal and gastric ulcers	37	12	32.4	16	8	3	37.5
Jejunal ulcer	87	56	64.4	10.7	42	26	61.9
Total	337	135	40	10.3	270	119	44.1

\* Operative mortality rate for 1940 is 4.1 per cent.

Follow-up studies were obtained in 36 of the 42 cases in which operation was performed from 1932 to 1936, inclusive. Prior to operation, there was an average of ten years of uncontrolled ulcer type of pain per patient. Twenty-seven patients gave a history of multiple hemorrhages, 13 of massive hemorrhage, five had hemorrhages within two weeks preceding operation, and six had less than 8 Gm. of hemoglobin per 100 cc. of blood on admission. Seven of the patients who had had massive hemorrhage were age 45 or more when this occurred. The various types of gastrectomy employed are listed in Table II.

TABLE II

TYPE OF PARTIAL GASTRECTOMY PERFORMED IN 112 TRACED PATIENTS WITH BLEEDING PEPTIC ULCER, 1932-1936, INCLUSIVE, AT THE MAYO CLINIC

Procedure	Duodenal Ulcer	Gastric Ulcer	Duodenal and Gastric Ulcer	Jejunal Ulcer	Total Cases
Billroth I.....	7	2	0	10	19
Posterior Pólya.....	28	17	10	30	85
Anterior Pólya-Balfour					
Without entero-anastomosis.....	1	0	0	2	3
With entero-anastomosis.....	0	0	0	3	3
Anterior Billroth II.....	0	1	0	0	1
Posterior Billroth II.....	0	0	0	1	1
Total.....	36	20	10	46	112

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TABLE III

RESULTS OF PARTIAL GASTRECTOMY FOR BLEEDING PEPTIC ULCERS, 1932-1936, INCLUSIVE AT MAYO CLINIC

	Total Cases	Cases Traced	Cases Not Traced	Hospital Deaths	Satisfactory Results			Unsatisfactory Results	
					Excellent	Good	Fair	Per Cent	Number
Duodenal ulcer...	42	36	3	3	25	7	2	94.4	2
Benign gastric ulcer.....	25	20	2	3	16	2	1	95.0	1
Duodenal and gastric ulcers...	12	10	0	2	7	2	0	90.0	1
Jejunal ulcer.....	56	46	4	6	22	6	7	76.1	11
Total.....	135	112	9	14	70	17	10	86.6	15

The results of partial gastrectomy for all bleeding duodenal ulcers show 94.4 per cent satisfactory results (Table III). The results were classified as satisfactory only if there has been no further hemorrhage nor symptoms of ulcer. Results were classed as excellent, when complete relief of symptoms

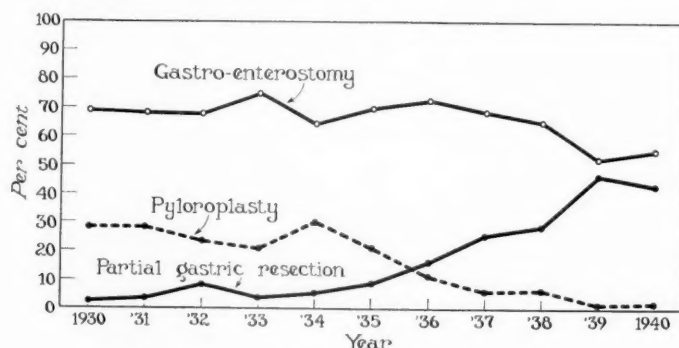


CHART 2.—Surgical treatment of duodenal ulcer.

was obtained; as good, when relief of the symptoms of ulcer was obtained but occasional fulness or sweating was present after meals; and as fair, when the symptoms of ulcer were relieved but more pronounced fulness after meals, sweating, or occasional vomiting occurred. In no instance did an ulcer type of pain or hemorrhage ensue. Results were classed as unsatisfactory whenever the patient had any ulcer pain or hemorrhage subsequent to operation, irrespective of whether it had occurred once, occasionally, or frequently. Unsatisfactory results were obtained in only two cases (5.5 per cent) in which resection was performed for bleeding duodenal ulcer. In each case, primary posterior Pólya-type of partial gastrectomy had been performed without removal of the pyloric antrum of the stomach. Multiple hemorrhages with ulcer type of pain occurred subsequently in both cases.

*Gastric Ulcer.*—From 1932 to 1936, inclusive, about 50 per cent of patients whose condition was diagnosed as benign gastric ulcer at the clinic were operated upon and for about 30 per cent of all the patients who had benign gastric ulcer, partial gastric resection was the operation employed. During this period 114 partial gastrectomies were performed for benign gastric ulcers, of which 25 (21.9 per cent) were hemorrhagic in character.

These statistics are comparable to those for the year 1940, in which 82 partial gastrectomies were performed for benign gastric ulcer, of which 17 (20.7 per cent) were bleeding lesions (Table I).

Two of the 25 patients who were subjected to partial gastrectomy for hemorrhagic gastric ulcer, in the years 1932-1936, inclusive, gave a history of massive hemorrhage. Twenty of these 25 patients were traced. Ninety-five per cent of these 20 patients attained satisfactory results (Table III). In 17 of the 20 traced cases, partial gastrectomy of the posterior Pólya-type had been performed; in two, the Billroth I procedure; and in one, an anterior Billroth II-type of resection without entero-anastomosis and with temporary jejunostomy (Table II). Only one patient (5 per cent) had an unsatisfactory result; a posterior Pólya-type of partial gastrectomy was performed for syphilitic gastric ulcer (serologic reactions were positive) in this case. There has been no subsequent bleeding but pain of an ulcer-like character has recurred.

*Gastric and Duodenal Ulcers.*—The results of partial gastrectomy for bleeding, concomitant duodenal and gastric ulcers, theoretically, should be comparable to those attained for bleeding duodenal or gastric ulcer. Such was the case in our series. Partial gastrectomy was performed in 37 cases, from 1932 to 1936, inclusive, for concomitant duodenal and gastric ulcers, of which 12 (32 per cent) were for bleeding ulcers (Table I). Of the ten cases of bleeding ulcer traced after partial gastrectomy, satisfactory results were obtained in nine (Table III). In the one case, in which the result was unsatisfactory, a posterior Pólya-type of partial gastrectomy was performed. A single, brief period of mild distress and mild hemorrhage occurred after operation, but since then the patient has enjoyed excellent health.

*Jejunal Ulcer.*—Of 87 patients treated by partial gastrectomy, from 1932 to 1936, inclusive, for jejunal ulcer, 56 (64.4 per cent) had associated hemorrhage (Table I). In 1940, 26 of 42 patients (61.4 per cent), treated by partial gastrectomy for jejunal ulcer, had bleeding lesions.

All but seven of the 56 patients who had hemorrhagic jejunal ulcers and were treated by partial gastrectomy, from 1932 to 1936, inclusive, had multiple hemorrhages prior to operation, and 15 had massive hemorrhage. Eight of the patients who had massive hemorrhages were more than age 45 when they occurred. Of the 46 traced patients 30 had been subjected to a posterior Pólya-type of resection (Table II).

Thirty-five patients (76.1 per cent) had satisfactory results (Table III). Eleven patients obtained unsatisfactory results. Ten of these 11 had subsequent hemorrhage, and ten had ulcer-type of pain. In six of the 11 cases, in which results were unsatisfactory, the Pólya-type of gastrectomy was performed. In four of these, the operations consisted of a posterior Pólya resection, and in two of these four cases, the pyloric antrum was not removed. In one case in which the pyloric antrum was not removed, death occurred from massive hemorrhage four years later, and in the other, pain, multiple hemorrhages and proved jejunal ulceration occurred. Of the other two

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patients who had been subjected to the posterior Pólya-type of gastrectomy, one had a single, mild, subsequent hemorrhage unaccompanied by distress, and one had one subsequent hemorrhage associated with occasional mild distress. In two cases in which results were unsatisfactory, an anterior Pólya-type of partial gastrectomy with entero-anastomosis was performed; in both, multiple hemorrhages and ulcer-type of pain occurred. In five of

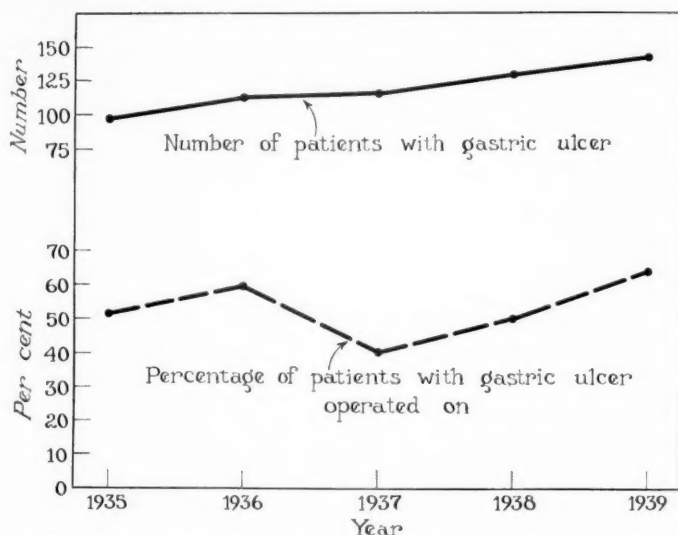


CHART 3.—Percentage of patients who had gastric ulcer treated surgically, from 1935 to 1939.

the 11 cases, the Billroth-type of resection was performed; in four, a Billroth I, and in one, a Billroth II. A single hemorrhage and ulcer-type of pain occurred subsequently in the latter case. One patient, who had undergone a Billroth I procedure, had two mild hemorrhages, associated with drinking; these were not accompanied by pain; one had pain without hemorrhage, and the other two, single and multiple hemorrhages with ulcer-type of pain. Interestingly enough, five of the 11 patients reported that they were in good health despite periodic evidence of ulcer.

*Analysis of Unsatisfactory Results.*—Ninety-seven (86.6 per cent) of 112 patients treated for bleeding peptic ulcer by partial gastrectomy, whom we were able to trace, obtained satisfactory results, that is, had no further episodes of hemorrhage or ulcer distress. It is exceedingly interesting to survey briefly the 15 unsatisfactory results (Table III).

Four (26.6 per cent) of the 15 unsatisfactory results occurred in cases in which the pyloric antrum and pyloric sphincter were not removed in the course of partial gastrectomy. In a total of seven of the 112 cases, the pyloric antrum was not removed, and an unsatisfactory result was attained in four of the seven (57 per cent). Both failures in cases in which the



primary resection was for duodenal ulcer, and two failures in the cases of jejunal ulcer presumably occurred on this account.

In the early experience with gastric resection, it was not appreciated that the pyloric antrum should be removed in all cases in which gastrectomy was performed for duodenal ulcer. Ogilvie,<sup>21</sup> out of 22 cases in which the pylorus was not removed at gastrectomy, found six cases of proved jejunal ulcer in a two-year follow-up study. In 100 cases of duodenal ulcer in which the pyloric antrum was removed at partial gastrectomy and in which follow-up study was made 12 years later, there were no recurrent ulcerations and only minor discomfort. Friedmann,<sup>14</sup> in 2,250 gastric resections, found jejunal ulceration in 4 per cent of his early cases and in only 0.5 per cent of the cases in the late group. In the latter group of cases a more radical resection, with removal of the pylorus, was carried out in all instances. The importance of removing the pylorus, if a maximal reduction of gastric acidity is to be obtained, has been confirmed experimentally by Wilhelm,<sup>31</sup> Crohn,<sup>9, 10</sup> E. B. Lewis,<sup>20</sup> and others (Table IV).

TABLE IV  
ANALYSIS OF UNSATISFACTORY RESULTS  
(13 per cent of cases)

Procedure or Explanation	Cases	Unsatisfactory Result	
		Cases	Per Cent
Pyloric antrum not removed.....	7	4	26.6
Entero-anastomosis.....	3	2	13.3
Billroth I.....	19	4	26.6
Syphilitic gastric ulceration.....	1	1	
No adequate explanation			
(Resection for gastro-jejunal ulcer in three cases).....		4	26.6
Total.....		15*	

\* Five of the 15 patients are in good health (three had single mild hemorrhage and two had two mild hemorrhages).

In 72 per cent of cases of duodenal ulcer, all cases of gastric ulcer, and many cases of jejunal ulcer at the clinic, a relative achlorhydria occurs when entero-anastomosis is not performed in association with partial gastrectomy. If entero-anastomosis is performed, marked reduction in gastric acidity is obtained only infrequently. Although a good functional result may not be dependent on a marked reduction of the gastric acidity, when there are unsatisfactory results it is noted that they occur in the group of cases in which a marked reduction of acidity has not followed. A good result was obtained in only one of three cases in which entero-anastomosis was performed as a part of the anterior Pólya-Balfour procedure, but in all three cases of gastrectomy with anterior Pólya-Balfour anastomosis without entero-anastomosis, results were good.

In four (26.6 per cent) of the 15 cases in which results were unsatisfactory, the Billroth I-type of resection was performed following removal of gastrojejunal stoma for jejunal ulcer secondary to duodenal ulcer.

In a study of the effect of various types of gastric resection on gastric acidity, one of us (Walters<sup>26</sup>) found that only 25 per cent of patients obtain

relative achlorhydria to the standard test meal after the Billroth I procedure for duodenal ulcer in contrast to 72 per cent after a posterior Pólya. It is interesting, therefore, to note that in the present study ulceration has recurred more frequently when the Billroth I-type of resection and anastomosis was employed.

In one case in which results were poor, the patient had a syphilitic gastric ulcer which was associated with hemorrhage; the partial gastrectomy relieved the patient of further bleeding but not of pain.

In the four remaining cases, there was no adequate explanation for the unsatisfactory results; three patients have been subjected subsequently to operation for jejunal ulcer, and one, for concomitant duodenal and gastric ulcers.

Five of the 15 patients, in spite of the classification of unsatisfactory result, are comfortable and report themselves to be in good health, although three had had a single, mild hemorrhage each; one, two mild hemorrhages; and one, one severe hemorrhage. Three also had occasional pain of the ulcer-type.

*Operative Mortality.*—The operative mortality in this study should not be considered as typical, except for the time-period in which the resections were performed. It represents an early period of experience in extensive partial gastric resection for benign ulcerating gastric, duodenal, and jejunal lesions and includes resections in that serious group of 56 cases of bleeding jejunal ulcers. There have been 14 postoperative deaths in the group of 135 cases of bleeding peptic ulcers, a mortality rate of 10.3 per cent (Table III). Three deaths (7 per cent) occurred in the 42 cases in which resections were for bleeding duodenal ulcer. Of the 14 deaths, eight were from peritonitis; five, from bronchopneumonia; and one was sudden, from an indeterminate cause, the third day following a second resection for recurring gastrojejunal ulceration. Two of the eight deaths from peritonitis followed gastric resection for acute ruptured gastric and duodenal ulcers associated with hemorrhage, and one was from peritonitis following resection for hemorrhagic gastrojejunocolic fistula.

In recent years, with better understanding of the contraindications for partial gastrectomy, and with improvement in preoperative and postoperative care, the operative risk has been reduced considerably.

In 1938,<sup>29</sup> there were 215; in 1939,<sup>18, 22, 27</sup> 352; and in 1940,<sup>30</sup> 300 patients were treated by partial gastrectomy for benign lesions of the stomach and duodenum, with a mortality of 2.8, 3.4, and 2.3 per cent, respectively. In 1940, there were 119 partial gastrectomies for bleeding peptic ulcers with five deaths, a mortality rate of 4.1 per cent. All of the deaths occurred in the 73 cases in which resections were for bleeding duodenal ulcer, a mortality rate of 6.8 per cent. Two of the five deaths occurred in cases of massive hemorrhage from duodenal ulcer, in which operation was undertaken more than 48 hours after the onset of bleeding.

## SUMMARY AND CONCLUSIONS

Ninety-seven (approximately 87 per cent) of 112 traced patients treated by partial gastrectomy for bleeding peptic ulcer obtained satisfactory results, without further hemorrhages and with relief of the ulcer-type of distress. One patient had a fatal postoperative hemorrhage. If cases in which the pylorus was not removed or in which entero-anastomosis was performed are excluded, then the satisfactory results reach 91.5 per cent. Of the 13 per cent of patients whose results were classified as unsatisfactory, six (5.4 per cent of the total) were living reasonably normal lives at the time this study was made, although evidence of recurrent ulceration had been present at some period.

Satisfactory results without subsequent hemorrhage or without subsequent ulcer-type of pain were obtained by partial gastrectomy in 94.5 per cent of bleeding duodenal ulcers. All primary resections for bleeding duodenal ulcer relieved the patients except the two in which the pyloric antrum was not removed.

Ninety-five per cent of patients treated by partial gastrectomy for bleeding gastric ulcer obtained satisfactory results. Five per cent had further pain; none had further hemorrhage. In all these cases, entero-anastomosis was not performed and the pyloric antrum was removed at operation.

Seventy-six and one-tenth per cent of patients who had bleeding jejunal ulcers and were treated by partial gastrectomy obtained satisfactory results. Seventy-eight and three-tenths per cent had no further hemorrhage, and one (2.2 per cent) had further pain without hemorrhage. In 8.8 per cent of the cases of bleeding jejunal ulcer, entero-anastomosis was performed with the gastric resection or the pyloric antrum was not removed; subsequent ulcer-type of pain and bleeding occurred in all. In an additional 8.8 per cent, Billroth I-type of resection was performed for bleeding jejunal ulcer, and subsequent bleeding and ulcer-type of pain occurred.

The pyloric antrum should be removed in the course of all gastric resections for bleeding peptic ulcer, but entero-anastomosis should not be performed because it tends to prevent a maximum reduction of gastric acidity.

From 1932 to 1936, inclusive, the risk of partial gastrectomy for bleeding peptic ulcer was 10.3 per cent in the 135 cases. In the 42 cases of bleeding duodenal ulcer it was 7 per cent. In 1940, the risk of partial gastrectomy for bleeding peptic ulcer was 4.1 per cent of 119 cases; for bleeding duodenal ulcer it was 6.8 per cent of 73 cases, and there were no deaths among 46 patients who had partial gastrectomies for 17 bleeding gastric, three bleeding gastric and duodenal, 25 jejunal, and one bleeding gastrojejunal colic fistula-type of ulcer. The improvement in operative risk has been attained by improvement in preoperative and postoperative care, the use of chemotherapy, a better understanding of vitamin deficiencies, more rigid indications for partial gastrectomy, and improvement in the postoperative care of pulmonary complications.

Our results support the contention that partial gastrectomy offers the best chance of cure or amelioration of symptoms of bleeding peptic ulcer and the best prophylaxis against further hemorrhage.

With elimination of procedures which have proved of least merit, such as failure to remove the pyloric antrum with the resected portion of the stomach, and entero-anastomosis, and with the less frequent use of Billroth I-types of procedures, results should be improved. Thus, in the 119 cases in which resections were performed for bleeding peptic ulcer at the Mayo Clinic in 1940, the pyloric antrum was removed in all but one case, and the posterior Pólya-type of resection and anastomosis was employed in 94.1 per cent. The results for 1940 should be superior to the 1932- to 1936-period, when seven pyloric antra were not removed, and only 75 per cent of the partial gastrectomies were of the posterior Pólya-type.

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- <sup>28</sup> Walters, Waltman, and Sebening, Walter: A Comparison of Lesions Associated with Duodenal Ulcer in Germany and in the United States. *Minnesota Med.*, **15**, 579-584, September, 1932.
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DISCUSSION.—DR. JOHN V. BOHRER (New York, N. Y.): This has been a most interesting and convincing paper on this difficult and controversial question. For many years, ulcer therapy has been in a state of flux. When it was accepted that peptic ulcer is best treated conservatively, many of the internists and gastro-enterologists failed to differentiate between peptic ulcer as such, and the complications of peptic ulcer. It is here that Doctor Walters' paper is of most value.

He has shown us a large series of ulcer cases complicated by bleeding. These patients have been operated upon, and an adequate follow-up has revealed a very satisfactory result. It is certainly most convincing and timely.

The statistics presented by Doctor Walters on the acute, massive gastric hemorrhage are of particular interest. He stated that in patients above age 45, treated conservatively, there is a mortality between 30 and 40 per cent. Our statistics from the Knickerbocker Hospital confirm this figure.

Permit me to present some statistics that have been collected both from the Knickerbocker Hospital records and from a questionnaire sent to the members of this Society.

During the ten-year period, there were approximately 41,000 patients admitted to the Knickerbocker Hospital, 456 for ulcer, of those 182 for bleeding, and 80 were classified as massive gastric hemorrhage. Massive gastric hemorrhage was defined as a patient with two million or less cells, and 35 per cent hemoglobin or less, this being accepted as a base line as no patients died above that level. There was a mortality of 17.5 per cent for massive gastric hemorrhage, or 7.6 per cent if computed on the entire bleeding group, or one death in every 3,100 patients admitted.

During the last two years, four patients have been operated upon during the bleeding period, two were delayed, and two were operated upon within a 48-hour period. All recovered. One died of pneumonia ten days postoperatively. It is just possible that the



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application of chemotherapy in massive doses intraperitoneally might be a prophylactic for postoperative pneumonia.

In all, there were 1,556 cases studied. In the hospital group, there were approximately 1,000 cases with a modest mortality of 11.3 per cent. That is probably due to a less rigid classification of massive gastric hemorrhage.

There were 548 patients treated conservatively, with a 16.7 per cent mortality, but those above age 45 in the gastric series had a mortality of 20.3 per cent, while the duodenal group had a mortality of 21 per cent. While it is recognized that the older patients, those above age 45 with massive gastric hemorrhage, have a much higher mortality, your attention is called to those of the gastric series—48 patients with nine deaths, or practically a 20 per cent mortality. Thus we cannot entirely forget the younger patients with gastric ulcers.

One hundred and twelve patients were operated upon with subtotal gastrectomy, with a 17.8 per cent mortality. This line really should read "with 82 per cent living," because most of these patients were operated upon as medical failures.

There were 48 patients operated upon by various operations, such as gastroenterostomy, ligation, local resection, *etc.* Seventeen died, a mortality of 35.4 per cent. Obviously, subtotal resection is the operation of choice.

Seventy-five marginal ulcers were reviewed, with a gross mortality of 8 per cent, 15 were reoperated, three having a subtotal gastrectomy, with one death. Sixty were treated conservatively, with five deaths.

The ulcer that is lethal, if treated conservatively is the one with an open vessel in the center of the crater surrounded by scar and granulation tissue. In most instances, spontaneous cessation is impossible and operation is necessary, within the 48-hour period to prevent a mortality.

DR. FORDYCE B. ST. JOHN (New York, N. Y.): May I enter a plea with Doctor Walters to continue the follow-up in these cases indefinitely. We have a dictum in our Peptic Ulcer Follow-Up Clinic, which is now 25 years old, as follows: "Never discharge an ulcer case from the Follow-Up Clinic." Thus, the follow-up record is preserved in continuity. Although, at times discouraging, it has proved most informative. The general excellence of the immediate and late results of subtotal gastrectomy with peptic ulcer, with persistence or complications, is a matter of factual record in any well organized surgical follow-up clinic. We have people, however, in our clinic (now representing a small but real percentage of complications), even after a ten-year follow-up period with no trouble, who have developed symptoms. It is but fair to add, however, that in many of these cases, especially the earlier ones, the actual amount of stomach which has been removed is difficult to determine, and in others, it is evident that a true subtotal gastrectomy has not been performed.

A verbal communication from another large clinic in New York is to the effect that they have had, and are having, a similar experience, and even in some cases where a technically satisfactory subtotal gastrectomy would seem to have been performed.

DR. ARTHUR W. ALLEN (Boston, Mass.): In 1933, Doctor Benedict and I published a study of the cases of massive hemorrhage from duodenal ulcer occurring in our hospital. We found that there had been one death in a man, age 25, from hemorrhage; another death in a woman, age 35; and two other males in the late forties had died. These were from a group of 90 patients under age 50.

In 42 patients over age 50, admitted during that same period of time, the mortality rate from hemorrhage was 33.3 per cent.

I have just checked the data from 1933 to January 1, 1941, in our hospital, and found that there have been 80 cases of acute, massive hemorrhage from duodenal ulcer during that eight-year period. Modern methods of treatment, such as feeding the patients early, and administering continuous transfusion, have been employed. There have been nine deaths from hemorrhage in the 80 cases. All of those patients who died were over age 50, except one, and that patient was age 44.

Last week, a man, age 30, on our service, died of massive hemorrhage from duodenal ulcer. At autopsy, an entire segment of the vessel, running behind the duodenum, was found eroded away.

In other words, the mortality rate in the younger patients from hemorrhage is quite low, lower perhaps than we can match by an immediate surgical procedure.

In the older age-group, we have operated upon some of these patients during the early hours of bleeding; seven such patients have survived the procedure, and one died. All patients in this group were beyond age 50, except one. I do not believe we will have the opportunity, in our institution, to prove whether one can operate upon a very large group of acute, massive hemorrhage cases in the younger patients with as low a mortality rate as we have in those operated upon at the time of election.

Our experience with operation upon bleeding ulcers at the time of election corresponds very closely to that of Doctor Walters. Our group has not been so large, but we have learned definitely, namely, that we cannot leave the antrum of the stomach behind without having further trouble. Five out of seven cases treated in our clinic by the "resection for exclusion" method, have developed subsequent ulcers. Fortunately, most of our resections have included the antrum or antral mucosa, and the results have been good, when this has been done.

Doctor McKittrick has been very much interested in "staging" the procedure of subtotal gastrectomy in difficult cases. By dividing the antrum and proceeding with proximal subtotal resection as a first stage, and then deliberately going back six weeks later and removing the pyloric segment. This seems to me to satisfy a great many of the objections to the more radical one-stage procedure on these deeply adherent ulcers during their acute phase or when the inflammatory reaction is so great.

DR. ROSCOE R. GRAHAM (Toronto, Can.): I was disturbed by Doctor Zininger's suggestion that we are to operate as an emergency upon cases of massive gastric hemorrhage. The survey of our own group revealed 136 cases of duodenal ulcer with the criterion of gastric hemorrhage being an hemoglobin drop to 50 per cent or less. None of these was operated upon. The mortality was 7 per cent. With one exception, I think all the cases that have been operated upon in our own hospital have died when treated as an emergency.

DR. JOHN A. MCCREERY (New York, N. Y.): I would like to speak for a moment in regard to Doctor Walters' paper, particularly with reference to the marginal ulcers. He has done us a favor in bringing to our attention the importance and frequency of massive hemorrhage in this group of cases.

We are apt to think of marginal ulcers as characterized by intractable pain and, in the late stages, going on to the development of a gastrocolic fistula. I was surprised at the frequency of hemorrhage in Doctor Walters' statistics, but in looking up my own cases from the First Division of Bellevue, found that 10 per cent of our marginal ulcers had at some time had a massive hemorrhage. I do not agree with Doctor Walters in his preference for the posterior anastomosis, feeling that the anterior route has, at least in my hands, been more satisfactory. It seems to me that with the anterior procedure we can take out more of the lesser curvature, and that a relatively aseptic operation can be performed without clamps, and with perhaps a little less chance of leakage at the anastomosis.

Our experience in follow-up in these cases coincides with that of Doctor St. John; but at Bellevue the question of the economics of follow-up in a city hospital becomes of importance. I have tried to follow-up our gastric cases for seven years, feeling that if we can carry them through that length of time without symptoms we might feel that they were cured. Recently, however, a patient upon whom a gastro-enterostomy had been performed 19 years ago, and who had been followed for seven years in the clinic, came back with a six months' history of pain, and was found to have a marginal ulcer which had developed after 18½ years of complete relief following his gastro-enterostomy, so perhaps we should follow these cases indefinitely.

One point in Doctor Allen's paper which I would like to stress, is the importance of the Wassermann reaction, or rather the importance of not relying on it too seriously. Wassermanns are done as a routine on our Service, but it has been our experience that true syphilis of the stomach is a rare disease, and that gastric lesions in patients with positive Wassermanns have been more apt to be benign or malignant ulcers in patients with syphilis, rather than true syphilitic ulcers.

DR. FRANK H. LAHEY (Boston, Mass.): These are both very interesting papers, and it seems to me that there is a good deal to be learned from each of them.

To deal with the first one, it is interesting to note in all the clinics the progressive

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change in the percentage of operative cases. In just short of 5,000 duodenal ulcers, we have operated just short of 7 per cent. In 380 gastric ulcers, we have operated upon 27 per cent. That, I think, represents about the attitude to-day regarding the surgical treatment of ulcers.

There is one thing I would like to relate, based on my own personal experience in the way these cases are operated upon for hemorrhage. There will be a tendency, I think, to undertake conservative types of resections, particularly the Finsterer resection by exclusion, in the cases of ulcers operated upon for bleeding, because these ulcers are active, indurated, and penetrating, and particularly because they are so often close to or adherent to the common duct. Furthermore, they shorten the duodenum and make one think the ulcer is adherent more closely to the common duct than it really is. Until one has had considerable experience in mobilizing these active ulcers, he tends to assume that it would be too dangerous from the point of view of possible injury to the common duct to remove them. This is, I think, a mistake. In very few cases will it not be possible to mobilize these ulcers so that they can be removed, and then the disadvantage of leaving behind the part of the duodenum containing the ulcer or the lower end of the stomach in resection by exclusion of fistula will not occur.

The technical procedure which makes this possible, based upon our experience, is the approach to the duodenum from below the common duct, rather than from above. If you attempt to mobilize the duodenum by approaching it from above, you will be in constant dread of opening the common duct. If you mobilize it well from below, turn it over and demonstrate the common duct from behind; from its posterior aspect where it is not involved in the exudate, it will be possible to remove the ulcer safely, leaving a portion of the duodenum, and it can be done in practically all cases.

Let me say, in regard to the antecolic anastomosis without entero-enterostomy, I did this because I admit a jejunal ulcer may occur in the stump of the stomach. If an antecolic anastomosis without entero-enterostomy is done, it will be easy to handle. Furthermore, the idea of not doing enterostomy is a sound one. I can say it can be done safely from the number we have performed.

Our mortality has decreased remarkably. I could not help but think of it when we talked about carcinoma of the colon this morning. The mortality in an operation will decline on one basis, that of a large experience. The whole principle of low mortality rates in these extensive operations of resection of the stomach or of the colon and rectum involves one sound factor, that is that they are difficult operations and they can be made safe only by giving them to a few men to do. If you spread them out, as is true of less serious operative procedures, the mortality will be high, but if you give them to a few men in clinics to do, as they become familiar with them, the mortality will be lowered.

As evidence of the lowered mortality rate, in the first year when we did subtotal gastrectomy for ulcer, our mortality rate was 18 per cent; in the second year it was 11 per cent, and we have now done 154 subtotal gastrectomies for ulcer with but one fatality and that a pulmonary embolus. That these are not selected cases but represent true mortality rates is proven by the fact that included in this group were 36 gastro-jejunal ulcers requiring resection of the jejunum in addition to the subtotal gastrectomy, and three gastrojejunal fistulae requiring resection also of the ascending and transverse colon.

I was worried about Doctor Allen's paper, but knowing his sound judgment I should have known better. I was worried that he would take the position that every gastric ulcer should be resected. That I think is a dangerous position, and the mortality from promiscuous resection would be high. After listening to his paper, I would agree with practically everything he said. I think it is very sound in principle, and I think all of these criteria are sound, and by them we may improve the results in resections for carcinoma of the stomach, which to-day are, of course, so distressing to us all.

DR. M. M. ZINNINGER (Cincinnati, Ohio): It has been a great privilege to hear Doctor Walters' paper which shows so clearly that bleeding ulcer can be so satisfactorily treated by resection, a fact which many of us have believed, but which we have not been in a position to prove statistically. With his large series and excellent follow-up, he has been able to show it. My experience with bleeding ulcers has, of course, been much smaller than Doctor Walters', but, in general, it agrees closely with his. At Cincinnati, we see a good many patients with bleeding ulcer who enter the hospital

during or immediately following a massive hemorrhage, and it is about the management of this type of case that I wish particularly to speak. During the period 1933-1936, 33 such cases were admitted to the Cincinnati General Hospital. None was operated upon during the period of active bleeding. Six died of uncontrolled hemorrhage, a mortality rate of 18 per cent. During the years 1937-1940 inclusive, 92 patients were admitted with massive hemorrhage diagnosed as due to bleeding ulcer with ten deaths, a mortality rate of 10.87 per cent. We believe that the reduction in mortality rate during the second of these periods was due to better medical management, plus the fact that some of the patients were operated upon during the period of active bleeding and the bleeding controlled surgically. Though it has been shown that operation is a life-saving procedure in some of these cases, the selection of patients and the choice of time for operation are points which are not yet entirely agreed upon. Many of our patients had not been under observation before they came in with acute hemorrhage, and often the source of bleeding could be determined only with difficulty. We have made use of roentgenograms by the Hampton technic in this sort of case when bleeding persists, and recommend operation if an ulcer can be demonstrated. In cases with known ulcer who have been under treatment, we believe that if massive hemorrhage occurs, operation should be carried out promptly, not waiting for a second or third hemorrhage, especially if the patient is age 45 or older. Table I shows my personal experience with the surgical treatment of such lesions during the past four years.

TABLE I

Cases	Color Sex Age	Operation No. of Days after Adm.	In Shock No. of Times	Procedure	Result
1.....	W. M. 58	50	5	Ligation of vessels entering gastric ulcer	Well 1 yr.
2.....	W. F. 41	13	3	Ligation of vessels entering gastric ulcer	Died 2½ mos. Acute liver atrophy
3.....	W. M. 54	2	2-	Partial gastrectomy for duodenal ulcer	Well 2 mos.
4.....	B. M. 29	7	3	Partial gastrectomy for duodenal ulcer	Died on table
5.....	W. M. 53	2	2	Partial gastrectomy for gastric ulcer	Well 2 mos.
6.....	W. M. 60	3	4	Partial gastrectomy for duodenal and gastric ulcer	Died 14 days. Pneumonia
7.....	B. M. 67	14	Almost continuous	Bleeding point not found	Finally ceased bleeding. Well 3 mos.

As can be seen, some of the gastric ulcers were treated by ligation of vessels, others by resection, while all duodenal ulcers were resected. Only two were operated upon within 48 hours of admission, both of whom recovered. The second case probably should not be included, as it seems likely that this was a carcinomatous rather than a simple ulcer, since a Kruckenberg tumor of the ovary was removed from this patient about two months later. The seventh patient also should not properly be included because no ulcer was found and the bleeding was not controlled surgically. He is included here because he was operated upon with the preoperative diagnosis of bleeding duodenal ulcer.

In addition to these cases—only five of which were proven ulcers—three others were operated upon by members of the resident house staff during this same period. All three of these died, one of pneumonia on the fourth day, the other two on the operating table. Death on the table is a most unfortunate accident, which indicates either too long a preoperative delay or poor judgment in selection of cases.

Three slides were here shown of drawings of resected specimens showing the thick-walled vessel in the base of the ulcer, with the eroded hole in the vessel plugged only

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with a soft blood clot—the same type of lesion as is seen in cases at autopsy after uncontrolled bleeding. It seems clear to me that with such a pathologic condition present, spontaneous cessation of bleeding cannot be expected to occur regularly, and that in some of these cases operative control of the hemorrhage will be necessary. The high mortality in our group of patients with operation, we believe, is due to the fact that we have not had an opportunity to operate as early as we would have wished, but only after conservative treatment had been found to be ineffectual. We believe that all these patients operated upon with ulcer would have died of uncontrolled hemorrhage without operation.

DR. WALTMAN WALTERS (Rochester, Minn., closing) : Eight years ago, it was more or less accepted, I believe, although a few physicians did not agree, that a trial course of medical treatment should be instituted in all cases of gastric ulcer. I am very happy to see that opinion change. The reason for this change, I think, is recognition of the fact that a carcinomatous lesion is present in a definite percentage of cases in which the roentgenologist makes a diagnosis of gastric ulcer.

A review of all our cases of cancer of the stomach in which operation was performed from 1907 to 1938, inclusive, has been made at the clinic, and two very interesting findings, among others, have come out. The first is that in 10 per cent of the cases of malignant lesions of the stomach in which resection was performed, the lesion had been reported by the roentgenologists to be gastric ulcer. Although the presence of a gastric lesion was recognized on roentgenologic examination in 99 per cent of cases in the series, recognition that it was a definite cancer was possible in only 75 per cent of the cases. These same statistics held for 1939, except that in 7 per cent of cases of cancer of the stomach in which resection was performed, a diagnosis of gastric ulcer had been made on roentgenologic examination.

The most disastrous observation in regard to symptomatology in our 1907–1938 series, was that 30 per cent of the patients gave a history of an ulcer type of distress, and of this 30 per cent, 80 per cent, or four-fifths, responded to medical treatment.



## GASTRIC ULCER\*

THE SIGNIFICANCE OF THIS DIAGNOSIS AND ITS RELATIONSHIP TO CANCER

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FROM THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

GASTRIC AND DUODENAL ULCER have been discussed so frequently under the general heading of "Peptic Ulcer" that a serious confusion has resulted regarding the proper management of these two distinct entities. Early symptoms in both diseases are much alike and the conservative measures, found adequate in uncomplicated duodenal ulcer, will also be temporarily effective for gastric ulcer. The greater frequency of acute duodenal lesions, compared to those in the stomach, has enhanced the standardization of the treatment of duodenal ulcer. This regimen applied to the more rare gastric ulcer has often proved disastrous. We believe that the time has come for a clarification of our ideas concerning the management of gastric ulcer and that every effort should be made to stress the seriousness of this lesion.

The difficulty in the differential diagnosis between ulcer and cancer of the stomach in our clinic has impressed us so forcibly that we feel justified in reporting our experience concerning the matter. We had already formed some ideas from certain cases falling into our hands for treatment but were surprised to find the evidence so clear to us when the available material was evaluated. The records of all patients, treated in our hospital during the ten-year period ending January 1, 1940, who have had the diagnosis of gastric ulcer, have been carefully analyzed for this purpose.

TABLE I  
GASTRIC ULCER  
*Error in Diagnosis of Cancer*

	No. of Cases	Per Cent
(A) Entire group		
Original diagnosis ulcer.....	277	
Final diagnosis cancer.....	39	14
(B) Patients treated medically*		
Original diagnosis ulcer.....	175	
Final diagnosis cancer.....	13	7.4
(C) Patients treated by gastro-enterostomy		
Postoperative diagnosis ulcer.....	23	
Cancer proved by follow-up studies.....	4	17
(D) Patients treated by resection*		
Preoperative diagnosis ulcer.....	69	
Cancer proved histologically.....	30	43

\* Several patients are included in both groups B and D.

This study deals with 277 patients whose original diagnosis was gastric ulcer (Table I). Thirty-nine of them, or 14 per cent, finally proved to have

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28, 1941.

# GASTRIC ULCER AND CANCER

cancer. Seventeen cases with a preoperative diagnosis of cancer proved to have benign ulcer. This makes a total of 255 cases of ulcer for analysis (Table II). The diagnostic methods were the usual ones employed in a large general hospital. The clinical diagnosis was based on the history, physical examination, and the laboratory data; this was confirmed by roentgenographic studies in all cases and by gastroscopy in many of them. When the ulcer was a large one or in one of the areas of the stomach where cancer is more likely (Fig. 1), or if there had been a poor response to conservative treatment, the patient was usually transferred to the surgical department.

In evaluating the percentage of error in diagnosis, each opinion was given its *pro rata* credit and no case, whose combined preoperative diagnosis was less than 50 per cent in favor of one diagnosis, was used in arriving at the diagnostic error. The opinion of the pathologist was accepted as final. In 69 cases subjected to gastric resection with a preoperative diagnosis of ulcer, 30, or 43 per cent, had a final diagnosis of cancer. In 18 of these patients, the error was made by all observers. In the remaining 12 cases, there was an opinion favoring the diagnosis of ulcer in from 50 to 90 per cent of those

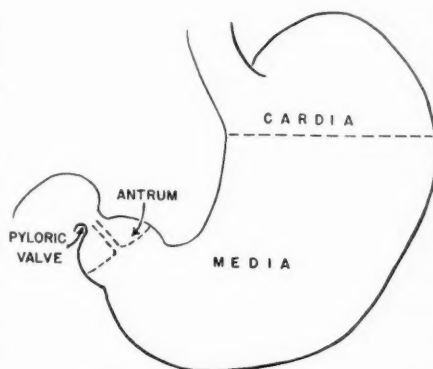


FIG. 1.—Anatomic divisions of the stomach.

TABLE II  
GASTRIC ULCER, 1930-1939  
Massachusetts General Hospital

Final Diagnosis Ulcer*	Cases	Deaths	Patients Dying in Hospital (Per Cent)
Medically treated			
1930-1934.....	59	3	5.1
1935-1939.....	103	4	3.9
Total.....	162	7	4.3
Surgically treated (acute perforations excluded)			
1930-1934.....	62	8	12.9
1935-1939.....	31	2	6.4
Total.....	93	10	10.7
Total cases.....	255	17	7.5

\* The original diagnosis of cancer was made on 17 of this group.

who participated in the management of the problem. If one wishes to take the most optimistic attitude and work out the percentage values on the basis of including only half of those cases where there was some divided opinion, the result is bad enough, since it is at best a 35 per cent error.

We have all performed radical gastric resection under the diagnosis of

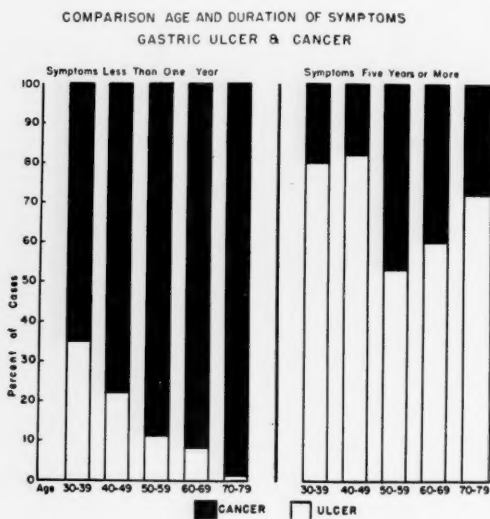
cancer, only to have the pathologist bring us the good news that the lesion proved to be benign ulcer. In the same decade of this study, 344 cases with a preoperative diagnosis of cancer that were either resectable or upon whom a palliative operation was possible, there were 17 with a final diagnosis of benign ulcer—a diagnostic error of 5 per cent. If we take our percentage error in both groups of cases into consideration, we still have much to be desired in the more favorable lesion for cure.

In 175 patients treated medically under the diagnosis of ulcer, 13 were eventually proven to have cancer—a diagnostic error in this group of 7.4 per cent. Twelve of them finally came to operation after an average interval of ten months from the original observation.

During the period covered in this report, 23 patients with gastric ulcer were treated by conservative surgery, usually gastro-enterostomy, with or without cauterization of the ulcer. Four of these patients later died of cancer, thus illustrating, more graphically, the difficulty of the surgeon to make a true diagnosis when the lesion is actually under observation. This is also a very strong argument in favor of partial gastrectomy when gastric ulcer is subjected to any surgical procedure.

Naturally, we have concerned ourselves with the reasons for our high percentage of diagnostic error when dealing with gastric ulcer. These factors were studied as follows: (1) The age of the patient and the duration of symptoms; (2) the location of the lesion; (3) the size of the ulceration; (4) the hydrochloric acid level of the gastric contents; (5) the rate of healing under medical therapy; and (6) the type of pain or discomfort complained of by the patient.

We expected to find that patients complaining of indigestion, hyperacidity, and gaseous eructations for the first time after age 50, would have cancer rather than ulcer. These data are illustrated in Graph 1. Here, we see that this is an important diagnostic point, since patients beyond the fifth decade, with a gastric ulceration causing symptoms of less than one year, are over five times as likely to have cancer as ulcer. On the other hand, those patients with symp-



GRAPH 1.

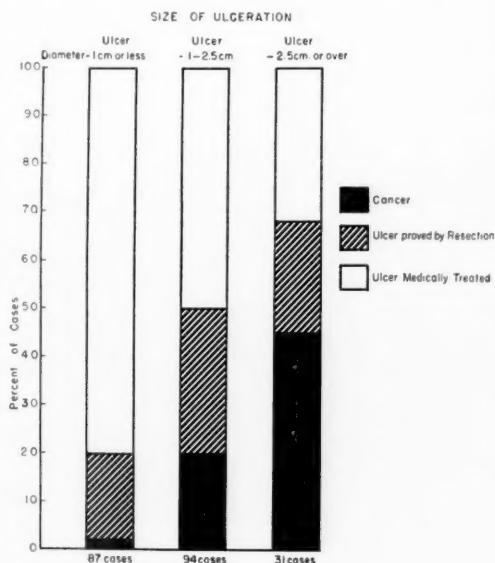
toms of five or more years have exactly the reverse ratio of ulcer to cancer. It seems evident to us, then, that conservative therapy in this older age-group has little to support it, nor is the incidence of ulcer in any group of cases great enough to make one certain he is not dealing with cancer.

# GASTRIC ULCER AND CANCER

That ulcerative lesions in some locations in the stomach are more likely to be cancer has been well-established. Holmes and Hampton<sup>1</sup> have previously stressed this point. In the group of cases under discussion, we have represented the percentage values in Figure 2. We have no difficulty in making up our minds regarding the treatment of ulcerative lesions arising in the fundus and in the prepyloric regions of the stomach, since the chance of cancer so far outweighs the risk of surgery. In the more common site on the lesser curvature, where 50 per cent of all gastric ulcers occur, we have been prone to feel safe on the basis that most of these lesions are benign. However, we actually find many of our mistakes in diagnosis are in lesser curvature ulcers. Thus, the physician, believing that this peptic ulcer will behave like others, fails to take into consideration the possibility of cancer. He then neglects to keep such a patient under observation until the lesion is completely healed, and he often is not actually aware of the true situation until the opportunity for cure is entirely lost.

The size of the ulceration is of some importance, and this is illustrated in Graph 2. In only two of our cases, with final diagnosis of cancer, was the lesion under 1 cm. in diameter.

The incidence of cancer increases progressively with the diameter of the ulcer. The majority of lesions over 2.5 cm. in diameter, proved by resection, turn out to be carcinoma. Between the diameters of 1 to 2.5 cm., the margin of error is such that not so much importance can be attached to the size. The average diameter of the benign lesion was 1.7 cm., while those showing cancer averaged 2.3 cm. The size of the crater then, although of some help in the differential diagnosis, is not a reliable guide. The margin of error is exactly 50 per cent in ulcerations of 2 cm. in size. One huge ulcer requiring total gastrectomy proved to be benign.



GRAPH 2.

The hydrochloric acid level has been taught for years to be an important differential diagnostic guide in gastric ulcerations. This is illustrated in Graph 3. Here, we see that acidity and cancer are compatible. An occasional benign ulcer will have achlorhydria, but it is clear that one should not often stress this possibility. It will be observed that the percentage of cases with free acid in the stomach is just as high with "ulcer-cancer" as it is with benign ulcer. There has been far too much emphasis on the acid

levels in relationship to the innocence of the lesion. A gastric analysis, negative for acid, is of help, but one with acidity is of no aid in the differential diagnosis between benign ulcer and cancer.

APPROXIMATE INCIDENCE OF CANCER IN GASTRIC ULCERATION

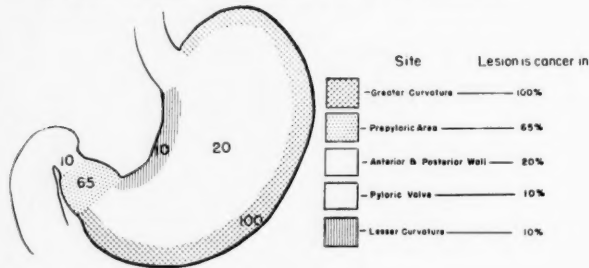
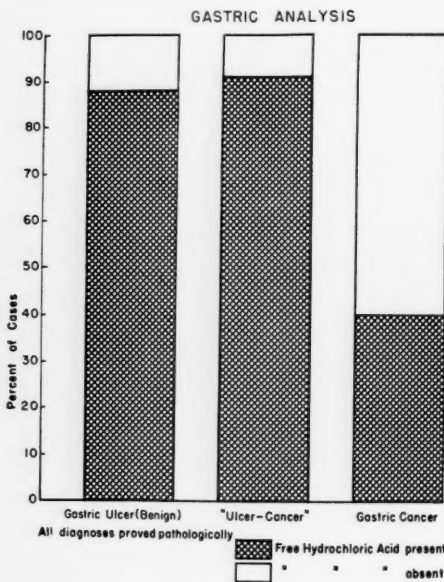


FIG. 2.

The rate of healing of gastric ulcers under medical supervision has interested us. Although it is not possible to graphically illustrate such a study, we have been able to form some opinion concerning it. In order to get a

base-line in regard to healing, we believe it is important that all patients with gastric ulcer should be admitted to the hospital for treatment, where conditions for cure can be made ideal and failure of the lesion to heal becomes of real significance. Too often, these patients are given the ambulatory advice handed out with impunity to patients with duodenal ulcer. The individual loses his symptoms and fails to return for a check-up. The physician then often interprets the absence of pain as such a favorable sign that he fails to insist on roentgenologic and gastroscopic confirmation of healing. Even when this is done, the report usually indicates a diminution in the size of the ulcer, and the impression is not made upon the patient regarding the im-



GRAPH 3.

importance of observations until complete healing has taken place. We have operated upon one patient with cancer and involved lymph nodes in a lesser curvature ulcer that completely healed after two months of medical therapy, according to roentgenographic and gastroscopic examination. Thus, it seems to us important that these patients should be followed under ideal hospital



management until complete healing has occurred. Even this cannot be construed as certain proof that the ulcer is benign, and such a healed ulcer should be again observed after a month's time as any evidence of recurrence demands surgery. If this program were insisted upon in this group of patients, a considerable number could be spared death from cancer. Of course, it is impossible to make a rule regarding the length of observation justifiable in all cases. We do feel however that, under proper conditions in the hospital, one should expect complete healing in one month if the lesion is benign.

The type of pain an ulcer of the stomach produces is not of as much importance as we thought it might be. We were of the opinion that the more vague the symptoms of indigestion, the more likely the lesion would prove malignant. Also, patients who have uncontrollable pain on a strict diet often prove to have cancer. On the other hand, it has been proved repeatedly that a decrease in the amount of pain occurring under treatment does not indicate that the ulcer is benign.

Although the physician is willing for his patient to submit to surgery, if he is convinced that the lesion is cancer, it is hardly to be expected that he should trust the surgeon with a benign ulceration of the stomach. This attitude has been brought about by the surgeon himself, since he has been slow in developing a sound surgical procedure for such lesions. Also, it has taken time and experience to evaluate methods that seemed in the beginning, for one reason or another, to offer cure in the majority of cases operated upon. The morbidity and mortality in this field of surgery has brought about a natural reaction on the part of physicians to evade the surgeon if possible. We believe now that we have evidence to warrant making a fresh endeavor to convince our medical colleagues that gastric ulcer should be fundamentally a surgical disease. We are willing that he continue to treat early, small ulcerations in the safer zones within the stomach, particularly in the younger patients. We do feel, however, that his treatment should be on a different basis than that used in duodenal ulcer. He should follow the patient with gastric ulcer until the lesion is completely healed and then check by roentgenograms and gastroscope at frequent intervals. He should be suspicious of any lesion that tends to recur or one that heals imperfectly within a short period of time. If he would take this attitude, in order to allow his patient to have an early and favorable operation for cancer alone, he would be justified in his position in the matter.

Under this regimen, a certain number of patients would have gastric resection for benign ulcer. Can the surgeon justify himself on this score? Our mortality figure of 6 per cent in a group of 53 primary resections may be representative since these are from a large teaching hospital, where many minds and many hands enter the picture (Tables III and IV). It is necessary to train surgeons and we do not defend such a mortality rate on any other basis. Personal series show even better results as do those from private clinics. There have been no fatalities in 36 resections for gastric ulcer in

our own personal cases, but this is beside the point. The internist must anticipate morbidity and mortality and the surgeon must be able to offset these difficulties if he makes a bid for these cases. In the 51 survivors from primary subtotal gastrectomy for gastric ulcer, we have only two patients

TABLE III

GASTRIC ULCER—SURGICAL THERAPY (M. G. H. 1930-1939)  
(Acute Perforations Excluded)

	No. of Cases	Deaths	Mortality (Per Cent)
Subtotal resection.....	56	5*	8.9
Posterior gastro-enterostomy.....	22	3	13.6
P. G. E. plus local excision.....	7	1	14.3
Local excision.....	6	1	16.7
Pyloroplasty plus excision.....	1	0	0
Total gastrectomy.....	1	0	0
Total.....	93	10	10.7

\* Two deaths occurred in patients who had had previous gastric surgery.  
Mortality of primary subtotal resection is 6 per cent.

TABLE IV

GASTRIC ULCER—SURGICAL THERAPY

	Resections	Other Operations	Total Cases	No. of Deaths	Mortality (Per Cent)
1930-1934....	30	32	62	8	12.9
1935-1939....	26	5	31	2	6.4

who have had recurrent symptoms. This is worthy of note when we consider the morbidity frequently associated with prolonged conservative treatment. At least 12 per cent of the patients under observation for gastric ulcer have had continued or recurring symptoms. Therefore, we feel that the results of proper surgery for gastric ulcer justify that form of therapy. This agrees with the conclusions of St. John, *et al.*,<sup>2</sup> based on meticulous follow-up data and of Walters and Clagett.<sup>3</sup>

Perhaps the strongest argument in favor of gastric resection for ulcer is based on the comparative data in Table V. In a group of 93 patients subjected to gastrectomy for cancer between 1932 and 1936, reported by Parsons and Welch,<sup>4</sup> from our clinic, we have an operative mortality rate of 25 per cent. Including these operative deaths, there were 20 per cent of five-year cures. In the small series that we can end-result, there were 30 gastrectomies performed under the diagnosis of benign ulcer—all of whom proved to have cancer. The operative mortality in this group was 10 per cent, and including these deaths, the five-year rate of cure was 40 per cent (Table V). Although we realize that the percentage values in so few cases are open to criticism, we believe it is fair to call attention to the likelihood of a lower mortality rate and a higher cure rate if the resection has been undertaken on the assumption that the lesion is ulcer and not cancer. In other words, the more

# GASTRIC ULCER AND CANCER

benign the lesion appears, the more likely the final cure. It is important to point out in this connection that the surgeon must have in mind the possibility of malignancy when carrying out gastrectomy for ulcer. The operation carries no more risk if the omentum and the lymph nodes of the lesser curvature are included in the resection. If this attitude is adopted in all questionable cases, the cure-rate will be even higher than 40 per cent in those having these early malignant lesions. This opinion is based on the fact that the nodal areas were not included in the resections for ulcer performed between 1930 and 1936.

TABLE V  
PROGNOSIS OF GASTRIC CARCINOMA  
All Cases of Resected Cancer      Preop. Diagnosis Ulcer  
(1932-1936)\*      (1930-1939)

Number of cases.....	93	30
Operative mortality.....	25%	10%
Five-year curability rate†..	20%	40%

\* Previously published.

† This is calculated from years 1930-1936, and includes operative deaths.

We recommend immediate surgery for any one of the following indications—if:

(1) The ulcer is of short duration and the patient is over fifty years of age.

(2) The ulcer is over 2.5 cm. in diameter.

(3) There is no free hydrochloric acid in the stomach.

(4) The ulcer is in the greater curvature or in the prepyloric region.

(5) The ulcer is chronic and on the lesser curvature.

We recommend hospital observation and treatment for one month—if:

(1) The ulcer is acute and in a young patient.

(2) The ulcer is under 1 cm. in diameter.

(3) The ulcer is on the lesser curvature or the anterior or posterior wall.

If healing is complete in one month, repeat observations should be made one month after discharge from the hospital.

If healing is not complete in one month, by roentgenologic and gastroscopic examinations, then surgery is advisable.

## CONCLUSIONS

Gastric ulcer is, fundamentally, a surgical lesion. This is the direct antithesis of our present concept regarding duodenal ulcer.

Gastric ulcer cannot be distinguished from cancer in a high percentage of cases.

The gastric cancers that simulate gastric ulcer comprise an especially favorable group for cure. On this basis alone, surgery should be the treatment of choice.

The end-results of gastric resection for ulcer seem to substantiate this same form of treatment even if the ulcer is proved to be benign.

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DISCUSSION.—DR. RALPH COLP (New York, N. Y.): The logical viewpoints expressed by Doctors Allen and Welch in their excellent presentation will probably meet with the full approval of those interested in this subject. Gastric ulcer, aside from its serious complications of hemorrhage, penetration, and perforation, presents the added hazard of the possibility of carcinoma, and the less likely danger of a carcinomatous transformation of an ulcer. Klein states the latter occurred only twice in a careful pathologic study of 141 cases of chronic ulcer.

In 1936, Dr. Percy Klingenstein reported all cases of chronic gastric ulcer, 165 in number, which were operated upon during a ten-year period (1925-1935) at the Mount Sinai Hospital, New York. The majority of patients gave a long-standing history of ulcer symptoms which ultimately failed to respond to medical therapy. There was a smaller group with an acute history, manifested by serious bleeding in 25 instances, and by signs of impending perforation in others. In over 20 per cent of these cases, a diagnosis of carcinoma was made by the roentgenologist, and 12 per cent, in which a benign lesion had been diagnosed clinically, were subsequently proven to be malignant.

For purposes of discussion, these ulcers may be grouped into those occupying the pyloric and prepyloric region; those situated at or near the reentrant angle and on the posterior wall of the stomach, and those located in the cardia. The lesions in the latter group of 29 cases were situated well proximal to the reentrant angle and some were juxta-esophageal. Many of these, as well as others, were complicated by adhesions to or penetration into the pancreas. A subtotal gastrectomy with removal of the ulcer was performed in 158 cases. The operative mortality was 15 per cent, contributed to mainly by cases with acute and serious gastric hemorrhages; by those with lesions in the cardia; and by those complicated by either previous gastric procedures, or long-standing pyloric stenosis.

During the past three and one-half years, Doctor Klingenstein and I have operated upon 28 consecutive cases of gastric ulcer. There were six other cases in which a benign lesion was suspected but in which a malignant one was found at exploration. We were not forced to operate upon any case with hemorrhage in the acute stage. We made it a rule to explore all prepyloric ulcers because, clinically, it is extremely difficult to differentiate between ulcer and carcinoma in this region. However, cases with pyloric stenosis were not operated upon until the blood chemistry determinations were normal.

A subtotal gastrectomy was performed in 23 cases, and a palliative gastric resection without removing the cardiac ulcers, the procedure advocated by Madelener and Florcken, was performed in five instances.

No one will deny that most gastric ulcers respond favorably to medical treatment, but, unfortunately, some malignant lesions, too, grow smaller under rest and appropriate diet. But in all cases, if certain well known and established criteria have not fully satisfied either clinically, roentgenologically, and by gastroscopic examination, after a three-week period of an ulcer cure, then surgical exploration should be insisted upon.

Subtotal gastrectomy is undoubtedly the operation of choice. It removes the ulcer radically, and if the case proves malignant, the chances of cure may be materially enhanced. Penetrating juxta-esophageal and high-lying ulcers, even if they do not respond to medical treatment, should be explored, but not radically resected. If they prove malignant, they are inoperable at this stage, and if they are benign, they will disappear following a palliative gastrectomy. The operative mortality in subtotal gastrectomy will be

reduced if these high-lying lesions and cases with acute hemorrhage are treated more conservatively.

The follow-up results in gastric ulcer are excellent, and are superior to those obtained from subtotal gastrectomy for duodenal ulcer. No recurrent gastric or gastrojejunal ulcers have been observed.

DR. WALTMAN WALTERS (Rochester, Minn.): The objections to a routine medical regimen in all cases of gastric ulcer are that in some of them the lesion, instead of being a small gastric ulcer, is in reality an ulcerating carcinoma, and in others the medical regimen has little effect on the ulcer. In about 10 per cent of cases, roentgenologic or gastroscopic examinations will not assist in the differential diagnosis between a malignant and a benign gastric ulcer. It has been said that a trial course of medical treatment serves as a diagnostic aid, for, if the patient is relieved of symptoms, if roentgenographic examination demonstrates that the ulcer has disappeared, and if blood disappears from the stools, then the lesion is benign. Clinical experience, however, has demonstrated that in some cases of malignant gastric ulceration these criteria may seem to be satisfied but that the lesion does not heal; it only *seems* to have done so, for, as Schindler has shown, the carcinomatous process may extend from the margin of the ulcer into the crater, obliterating it.

The incidence of malignant changes in gastric ulcers has been stated to be from 10 to 20 per cent. Walton said that the statistics of Stewart now are generally accepted. He concluded that in 9.5 per cent of cases chronic ulcer becomes carcinomatous and that carcinoma originates in a chronic ulcer in 17 per cent. Katsch, however, reported an incidence of 20 per cent. Finsterer found that in 532 cases of resection for gastric ulcer the ulcer was carcinomatous in 141, an incidence of 20.9 per cent. In the 1907-1938 series, reported from the Mayo Clinic by Doctors Walters, Gray and Priestley, 10 per cent of the carcinomata were reported as gastric ulcers and 1 per cent as benign lesions.

The risk of the operation for gastric ulcer should not exceed a maximum of 5 per cent, and it is possible to operate upon a large series of patients who have gastric ulcer with a mortality rate of considerably less than 5 per cent. In point of fact, in 278 cases in which partial gastrectomy was performed at the Mayo Clinic in 1939 for benign ulcers of the stomach or duodenum, the mortality rate was 4 per cent. Partial gastrectomy for gastric ulcer was performed in 89 cases, with a mortality rate of 2.2 per cent. In 1940, partial gastrectomy for gastric ulcer was performed in 88 cases, with one death. Excision or gastro-enterostomy or both were performed in 17 cases, with no mortality. The cases were selected carefully, and partial gastrectomy was performed only when the nature of the lesion and the condition of the patient warranted this procedure.

On reviewing 272 cases of chronic gastric ulcer in which operation was performed at the Mayo Clinic from January 1, 1933, to December 31, 1936, inclusive, Clagett and I found that 66.9 per cent of the ulcers were at or above the incisura angularis, 15 per cent were on the posterior wall, and 1.5 per cent were on the greater curvature. The remainder were below the incisura angularis.

In several of the cases at the clinic the ulcer appeared, on roentgenologic examination, to be located very high on the lesser curvature, and for this reason it was thought that operative removal would be difficult; it was found at operation, however, that perforation of the lesion to the capsule of the pancreas had given an erroneous idea of the amount of the stomach between the ulcer and the esophagus. In these cases there was actually much more uninvolved stomach than the roentgenogram indicated. On other occasions, the early division of the gastrohepatic omentum at a very high level assisted in mobilizing the upper part of the stomach so that unusually high lesions could be removed without too great difficulty.

During 1938 and 1939, at the Mayo Clinic, in 26 cases partial gastrectomy was performed for cardiac gastric ulcer, with one death, a mortality of 3.8 per cent.

I have referred to these cardiac ulcers because frequently I have seen patients with such lesions in whom the excuse for a course of medical treatment, even though the lesion was large, and in many cases had been complicated by hemorrhage, was that the lesion was probably located too high to be removed safely. The fallacy of this opinion is borne out not only by the fact which has been brought out, namely, that the lesions appear roentgenographically to be higher than they really are, but in a group of cases in which



such lesions were removed surgically, the operative mortality was only slightly higher than that for similar operations for gastric ulcer located at the lower levels on the lesser curvature or the body of the stomach.

In regard to some of the points on technic brought out in the discussion of Doctor Allen's paper, I sincerely believe that as time passes and anterior anastomosis after resection is performed in more cases, experience will show that posterior anastomosis is preferable in cases in which resections are performed for duodenal ulcer. My reason for this statement is my experience abroad, where many more resections have been performed for duodenal ulcer and the posterior method has proved the method of choice. Furthermore, in my own experience in cases in which the anastomosis is necessarily made anterior to the colon, because of the longer loop of jejunum used in the anastomosis, retention in that proximal loop develops in a definite percentage of cases, and entero-anastomosis has to be performed later. This procedure interferes with some of the physiologic-chemical effects of the operation, so that the reduction of gastric acidity is not as great. You will recall that 25 per cent of the unfavorable results in resections for bleeding ulcers which I reported were in cases in which entero-anastomosis was performed.

Theoretically, the Billroth I-type of operation should be an excellent type of operation. In selected cases of carcinoma, its results have been excellent and similar results can be expected when it is used in the treatment of gastric ulcer. When employed in the treatment of duodenal ulcer, it fails to produce a relative achlorhydria in 75 per cent of the cases, and the incidence of recurring duodenal ulceration is high. For example, on follow-up study in our series of bleeding ulcers, recurrent bleeding ulcers were found in four of 19 cases in which the Billroth I-type of anastomosis was employed. In 26.6 per cent of the 15 cases in the whole series, in which results were unsatisfactory, the Billroth I-type of anastomosis had been employed. It is true that these poor results occurred after resection for jejunal ulcers. It might be assumed that the Billroth I-type of anastomosis is the best type in such cases, but such has not been my experience. I have performed Billroth I resections in many cases for duodenal ulcer, gastric ulcer, and gastric carcinoma. The incidence, in my experience, of recurring ulcer after this type of operation performed for duodenal ulcer has been comparable to that following gastro-enterostomy. On the other hand, in the treatment of selected cases of gastric ulcer or gastric carcinoma it has a definite place and the results are equally as favorable as those from the Pólya-type of operation.

DR. FORDYCE B. ST. JOHN (New York, N. Y.): We are in complete accord with Doctor Allen's conclusions, in that we feel they represent a definite tendency in the right direction based on appreciation of potential dangers in ulcer of the stomach which are all too often missed until too late. We have had similar experiences because of our own errors in diagnosis, and that of our medical friends, the roentgenologist and the gastroscopist.

The newer problem of antral gastritis has introduced an "X" factor which may furnish potential danger in differential diagnosis.

Aside from these factors of danger, we should remember that, fundamentally, we are dealing in carcinoma of the stomach with a lesion, advanced on admission to most of our clinics, and in which, in the study of the biologic characteristics of this tumor, one must realize that about 66 per cent are of the invasive type, difficult to cure under any circumstances, and only about 33 per cent are of the so-called fungating type, or the more favorable lesion. In a study of 147 resections of cancer of the stomach at the Presbyterian Hospital, we had no cases of longevity in the invasive type, whereas in the more favorable smaller group, postoperative survivors were found living and well up to 23 years after resection.

DR. J. SHELTON HORSLEY (Richmond, Va.): Doctor Allen has very effectively presented the case of cancerous change in gastric peptic ulcers. This is peculiarly appropriate because at present certain gastro-enterologists are claiming that practically never is gastric cancer developed upon peptic ulcer.

Doctor Allen has given an excellent résumé of the probable changes from peptic ulcer to gastric cancer, but there are exceptions to all of those rules. I had a patient, a man age 31, who had what appeared to be a gastric peptic ulcer. The free hydrochloric

acid was 74°. He proved to have a small round cell carcinoma. He recovered from the partial gastrectomy, but eight months later had a recurrence, from which he died. Of course, this is exceptional, but the exception must be borne in mind.

Another patient, Mrs. L. E. H., age 70, had had gastric symptoms at intervals for about 15 years. A few months before entering the hospital, roentgenologic examination showed a defect in the pyloric end of the stomach. A partial gastrectomy was performed, December 10, 1928. There was a lesion on the lesser curvature about one inch from the pyloric sphincter. The ulcer was not deep but was somewhat infiltrating. Several sections showed the typical appearance of a peptic ulcer, some with regenerating epithelium and leukocytic infiltration. In one section, however, there were two adjacent acini that gave the typical histologic appearance of cancer. There were mitotic figures, a diaster, irregular nuclei, and invasion of the basement membrane. There can hardly be any disagreement as to the fact that the histologic appearance of these two acini showed cancer, and yet everywhere else that it was examined the histologic appearance was that of peptic ulcer. There appears to be no other logical explanation of this case, with the history of gastric disturbance for 15 years, than that the malignancy developed upon a peptic ulcer.

In regard to the treatment of peptic ulcer, I think in most cases a partial gastrectomy is indicated. If the ulcer is penetrating into the head of the pancreas, a type of Billroth I partial gastrectomy, which I have performed for many years, is suitable. The stomach can be divided about its middle between Payr clamps, the distal portion lifted up, and the penetrating ulcer is shaved off with a cautery along with a thin layer of adjacent pancreatic tissue. The stump of the stomach can then be brought over and attached to the stump of the duodenum more readily than this short stump of the duodenum can be closed. There are a few recurrences after this operation, but they can be treated more satisfactorily than a recurrence after a Billroth II-type of partial gastrectomy.

DR. ROSCOE R. GRAHAM (Toronto, Can.): I should like to present data showing the relation of the site of a gastric ulcer to carcinoma. In the personal cases operated upon, in which the lesion was definitely prepyloric, we found that 94 per cent were carcinoma, and only 6 per cent were benign. The group from the esophagus to the incisura showed 40 per cent malignant and 60 per cent benign. Thirty-five per cent of the latter had an organic hour-glass as evidence of their chronicity.

Singleton and Sommers, of the Roentgenologic Department of the Toronto General Hospital, studied a group in which there were 189 prepyloric gastric cancers, and during the same period they found 120 benign prepyloric ulcers. In the group of gastric cancer, ulceration was the only evidence of malignancy in 24, and in 17, or 85 per cent of those, the crater was less than 2.5 cm. in diameter. This supports Doctor Allen's contention that a small ulcer may be malignant, and justifies his suggestion that, even if the person be under age 50, he will operate upon a prepyloric ulcer under 2.5 cm. in diameter. There were eight cases in which carcinoma had probably developed upon a benign ulcer base. We are very anxious that all prepyloric ulcers be proven benign. This means excision, even though the ulcer be small.

## MASSIVE GASTRIC HEMORRHAGE: WITH SPECIAL REFERENCE TO PEPTIC ULCER\*

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KNICKERBOCKER HOSPITAL, with its large metropolitan ambulance service, offers many lessons in acute emergency surgery. Among these, massive gastric hemorrhage occupies a unique place in testing the diagnostic acumen of the surgeon and the facilities of the hospital to meet a real crisis. To witness rapid exsanguination by hematemesis is a most harrowing experience to both surgeon and patient. It is a combination of concealed or silent hemorrhage with all the evidence of the shock of external hemorrhage.

Penetrating ulcer is unquestionably the most common cause of this condition. Depending upon its location, hemorrhage may be totally concealed or, regardless of its site, bleeding into the stomach may take place, followed by hematemesis.

Before proper treatment, other than the emergency blood transfusion, can be instituted a differential diagnosis must be made. Usually, this can be determined by eliciting a history of gastric distress preceding the hemorrhage. Not infrequently, however, no such history can be obtained. Two cases are cited to illustrate:

A well-nourished woman, age 47, was admitted to the Knickerbocker Hospital in a state of severe shock following profuse hematemesis. No diagnostic history could be obtained, as she had always been well up to the time of the hemorrhage. Postmortem examination revealed an early cirrhosis of the liver with esophageal varices. A blood clot was found in the ruptured varix.

Contrast the above case with the following: G. G., a man, age 45, was admitted for massive gastric hemorrhage. He admitted taking an excess of alcohol and gave an indefinite history of previous gastric disturbance, especially while drinking. He continued to vomit blood. A diagnosis of esophageal varix was made but autopsy revealed a punched-out gastric ulcer with a fair-sized open vessel in its center.

While it is recognized that many other conditions, to be discussed later, cause profuse hematemesis, the differential diagnosis of the two diseases illustrated by these brief case reports will be first considered. In about 10 per cent of all cases of profuse gastric hemorrhage, the history and physical examination will be inconclusive. Certain stigmata point to the diagnosis of an early cirrhosis of the liver with a bleeding esophageal varix.

(1) Spider angiomata, usually on the face, neck and back, characterized by a central point from which radiate fine hair-like branches. The central point is frequently pulsatile. These angiomata may be obliterated by com-

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pressing the "body" of the lesion with a fine pencil point. There are also "mat" nevi, slightly elevated areas of skin of a reddish or purplish color, due to uniform distention of small venules.

(2) Slight enlargement of the spleen due to chronic splenic vein obstruction.

(3) The so-called liver palms, which consist essentially of a deep reddish to purplish tinge of the thenar and hypothenar eminences of both hands.

(4) Sparse or even absent axillary and pubic hair and a distinct tendency to a female distribution is common in males. (Forty per cent of all autopsied cases at Knickerbocker Hospital).

(5) Clubbing of the fingers.

(6) Offensive breath without any assignable local cause.

The following cases treated in the Knickerbocker Hospital presented many difficult problems in differential diagnosis.

**Case 1.**—T. McL., age 49, fireman, gave a history of profuse gastric hemorrhage two hours before admission. History and physical examination were inconclusive. Twelve hours after admission he had an exsanguinating hemorrhage. Blood pressure 60/40. He developed severe shock. He received 1,000 cc. of blood without further hemorrhage. Within 24 hours he had an upper gastro-intestinal roentgenologic examination, which was suggestive of cancer of the stomach. Later, exploratory celiotomy revealed a nonoperable adenocarcinoma which had ulcerated into a vessel of the transverse mesocolon.

**Case 2.**—G. L., female, age 45, was admitted for severe hematemesis. Roentgenograms showed a diaphragmatic hiatus hernia with a suspicious ulcer in the herniated area. Left phrenic paralysis, with elevation of the left leaf of the diaphragm has apparently cured the condition.

**Case 3.**—G. E., was admitted for massive hemorrhage, and gave a history of many attacks of bleeding during the past 20 years. Careful investigation, in another hospital, during these attacks failed to make a definite diagnosis of ulcer. Roentgenologic examination on admission showed redundant antral mucosa, which at times prolapsed through the pyloric ring. Operation confirmed this diagnosis.

**Case 4.**—G. D., female, age 68, had had a pylorotomy eight months previously for an ulcer, was admitted for exsanguination. Repeated transfusions were of no avail. Autopsy revealed a leiomyosarcoma of the stomach and the anastomosed jejunum, with metastasis in the liver. Pathologic examination of the pyloric tumor removed at previous operation failed to show a malignancy.

Hemorrhage from nonmalignant tumors of the stomach has been conspicuously absent in this group.

An analysis of Allen's<sup>2</sup> statistics of 2,031 cases places the bleeding from duodenal ulcers at 41 per cent, carcinoma 20 per cent, gastric ulcer 18 per cent, marginal ulcer 3 per cent, esophageal varices 16 per cent, and unverified 2 per cent.

*Frequency of Occurrence of Peptic Ulcer.*—During the ten-year period from 1931 to 1940, inclusive, 40,825 patients were admitted to the Knickerbocker Hospital, including 456 cases of peptic ulcer, of which 182 were admitted for gastric hemorrhage. Of 80 classified as suffering from massive gastric hemorrhage 14 died, approximately one in every 3,100, a mortality of 17.5 per cent. This accounts for the belief that massive gastric hemorrhage

is relatively uncommon and causes few deaths. In the Virginia Mason Hospital,<sup>33</sup> during a 20-year period, there was only one death from this cause for each 10,000 admissions to the clinic, a 15 per cent mortality. The ratio of the Knickerbocker Hospital group is much larger, due to an active ambulance service.

*Pathology of Bleeding Ulcers.*—Bleeding from an ulcer connotes activity even though hemorrhage is the first symptomatic evidence of its presence. Erosion of the mucosa may produce moderate bleeding and even superficial ulceration of the mucosa may occasionally cause massive gastric hemorrhage, although it is usually due to the erosion of a vessel of appreciable size.

The chronic penetrating type of ulcer may occur in any part of the stomach or duodenum. On the anterior and superior surfaces, a penetrating ulcer is more likely to perforate into the peritoneal cavity unless it becomes attached to a neighboring viscus. The general belief that perforating ulcers never bleed, is not true. Occasionally, erosion of a vessel in a viscus to which the ulcer has become attached and perforation at the periphery take place simultaneously. One such case was found in the Knickerbocker Hospital group and several were reported in the Questionnaire group. However, the posterior penetrating ulcer of the stomach or duodenum, with a necrotizing base in the head of the pancreas, is most provocative of massive gastric hemorrhage. In this location, a branch of the superior pancreaticoduodenal artery frequently becomes eroded. Such posterior peptic ulcers together with those on the lesser curvature, because of the proximity of the left gastric artery, account for most of the massive bleeding.

In the ulcer crater, the sclerotic artery is found terminating with an open stoma. The frequently described lateral stoma in a vessel running diagonally across the ulcer has not been noted. Found more frequently in patients above middle life, where arteriosclerosis is somewhat advanced, its mere presence in an ulcer crater, imbedded in granulation and scar tissue, is an important factor, regardless of the age of the patient, in keeping the stoma open. Chiesman<sup>11</sup> found a mortality of 74 per cent in a group of 62 patients who had bled for two or more days. Autopsy showed an open vessel in 45 of the 46 patients in this group. An eroded vessel in the crater of a chronic ulcer has frequently been found in the Knickerbocker Hospital group at operation or at autopsy. In the Questionnaire group, where autopsies or operations were reported, this was a common finding.

*Symptoms.*—A small percentage of ulcers belongs to the "silent" type in which perforation or bleeding is the first indication of their presence. Heavy lifting while at work, recent respiratory infections, or alcoholic excesses associated with emesis are frequent exciting causes.

If massive bleeding takes place, syncope followed by hematemesis or the passage of one or more bloody stools is not uncommon. Unfortunately, the initial symptoms rarely indicate the degree and extent of the hemorrhage. Fright also may be present, especially with the first hemorrhage, and the pallor of fainting is confused with true shock. The amount of blood lost is



usually grossly exaggerated by the patient or witnesses. Blood counts are deceptive if taken before replacement of fluid, as bleeding is quantitative and not qualitative. However, an accurate estimate of the severity of the hemorrhage may be made by the rapidity of the pulse, low blood pressure, and symptoms of shock. Without a definite history of ulcer, the actual cause of the hemorrhage, whether from esophageal varices, gastric polyps, carcinoma, gastritis, redundant gastric mucosa, or simple hemorrhagic diathesis cannot be made.

*General Management.*—All patients having gastric bleeding should be considered seriously ill and given absolute bed rest, with sufficient morphine to allay fear and restlessness.

(1) Pulse rate and blood pressure reading should be taken frequently and, if possible, by the same attendant, thus minimizing the personal error.

(2) Shock, if present or imminent, must receive appropriate treatment, ice caps to the epigastrium being definitely prohibited.

(3) As soon as possible, a Levine tube should be passed well into the stomach through the nostril for aspiration of liquid blood and lavage with saline until the stomach is free of blood clots. The removal of the blood from the stomach prevents nausea and vomiting and is of value in that a portion of the water passing into the intestines is absorbed. If, after the stomach is entirely empty, bright red blood continues to return through the tube, it is evident that hemorrhage is still active and is probably arterial, indicating immediate operation for its relief. The use of the Levine tube is, therefore, not only of therapeutic but of great diagnostic value. Soper<sup>31</sup> states: "I have encountered four cases in which early surgery was employed because of this appearance of the bright blood after lavage, and all four patients recovered. In each instance the surgeon located the spurting artery." As fine a record as that does great honor to the diagnostician and gives keen satisfaction to the surgeon, whose natural instinct is to ligate a bleeding vessel if he wishes to control hemorrhage.

The Levine tube may also be used for continuous or interval introduction of a liquid having acid combining power and a high caloric value.

To summarize the therapeutic value of the Levine tube:

(a) Severe straining and reverse peristalsis of the stomach is inhibited by removing the nauseating blood.

(b) Feeding is easily accomplished.

(c) The blood clot in the vessel is not mechanically removed either by vomiting, by peristalsis, or by the pangs of hunger. If lavage removes a friable clot, it is evidence of a useless clot that will not stop bleeding, such as is often seen in the throat after tonsillectomy.

(d) The ferments first removed with the blood by lavage are now combined with food and do not digest the ulcer, vessel, or clot. The Andresen<sup>4</sup> diet answers this requirement perfectly.

(e) The administration of adrenalin or various coagulants through the

tube may be of value in diffuse bleeding from gastritis but obviously is of little value in the presence of an open vessel.

(4) Roentgenologic examination during the bleeding period: Although in the past roentgenologic examination during this period has been strictly forbidden, the acceptance of the feeding therapy for bleeding ulcer now allows such investigation of the upper gastro-intestinal tract while the hemorrhage is still active. Admittedly, such an examination is incomplete. Manipulation and pressure tactics are omitted. These examinations have been made at Knickerbocker Hospital with satisfactory results. Esophageal varices, lesions of the stomach such as ulcer or polyps, and deformity of the duodenal cap have been diagnosed. The surgeon, however, must be prepared to operate should this initiate a secondary hemorrhage.

(5) Typing of blood and accessible donors are essential in all cases of massive gastric hemorrhage. This is particularly true in hemorrhage from an ulcer on the lesser curvature in which lethal exsanguination may rapidly develop.

(6) Diet is as important to prevent recurrent ulcer in the postoperative patient as it is for healing the ulcer in the conservatively treated patient.

Meulengracht,<sup>24</sup> and Andresen<sup>4</sup> were in the vanguard in urging a feeding regimen as opposed to the time-honored principle of starvation for bleeding peptic ulcers. Mortality statistics, as given by the advocates of these various diets, are especially difficult to understand. Meulengracht reports a mortality of only 1.0 per cent for his group of 231 cases, while La Due,<sup>20</sup> in a recent paper, reports a mortality of 1.3 per cent for his group of 81 patients treated by using the Andresen diet.

It is becoming generally accepted that a starvation diet, with an ice cap to the upper abdomen, should be abandoned. An acceptable diet that will absorb acid and prevent action of digestive juices on the ulcer and especially on the clot in the eroded vessel, is very important. However, it is very difficult to accept by ratiocination a difference in mortality of 1.3 per cent reported by La Due, who used the Andresen diet, with 14.5 per cent reported by Allen and Benedict,<sup>3</sup> using an initial period of starvation. In the Knickerbocker Hospital group treated conservatively, most of the patients were treated by the older method. At present, however, the Andresen diet is being used. Too few patients have been treated by the latter regimen to make a comparison.

(7) Transfusions and iron medication for the resulting anemia are not necessary, as rebuilding of blood is very rapid.

(8) Blood chemistry should be followed, urea nitrogen usually becoming normal soon after cessation of bleeding and replacement of circulating fluid. The decreased urea clearance is due to extrarenal azotemia rather than the mere presence of blood in the gastro-intestinal tube.

(9) The patient is rehabilitated by this procedure in from three to six weeks, depending upon the severity of the attack and his regenerative ability.

(10) The most important of the above outlined management is that it

offers a means of selecting the lethal bleeders in the first 12- to 48-hour period. Most of them will die if treated conservatively, and should have radical treatment while still good surgical risks.

(B) *An Indication for Operation.*—If continued bleeding is indicated by the syndrome of rapid pulse, drop in blood pressure, air hunger, slight delirium, reduced blood count, and hemoglobin, a transfusion sufficient to raise the blood count and hemoglobin a measurable amount should be given. If, after transfusion, the red cells and hemoglobin show a marked decrease within from one to 12 hours, it is certain that bleeding is taking place from an eroded vessel and immediate operation is indicated.

The value of a further decrease of blood count, notwithstanding transfusion, in justifying operative interference is well illustrated in the following case:

**Case Report.**—J. McE., male, age 34, was admitted to the Medical Service for profuse gastric hemorrhage, and was treated in the routine conservative manner. When hemoglobin reached 34 per cent, with 2,750,000 R. B. C., he received a transfusion. Forty-eight hours afterward, the hemoglobin and blood count had dropped below the previous level. He was again transfused, with practically the same result, hemoglobin declining to 32 per cent, with 1,800,000 R. B. C. He was given 1,000 cc. of blood, and an emergency subtotal gastrectomy was performed under local anesthesia, plus oxygen inhalations. A posterior penetrating duodenal ulcer was resected from the head of the pancreas, the bleeding vessel found and ligated. Convalescence was entirely uneventful.

It is noteworthy that the sense of pain is so diminished in these exsanguinated patients that local anesthesia is well tolerated.

*Transfusions.*—While transfusion of blood during an attack of massive gastric hemorrhage is now generally accepted, a small minority still believe that transfusion is contraindicated for the reason that by raising the blood pressure the clot in the bleeding vessel is dislodged, with consequent recurrence of the hemorrhage. No proof of this theoretic objection has ever been produced. On the contrary, there is much evidence to support the advantages of proper amounts of blood during the acute anemic condition.

(1) Severe grades of anemia are provocative of certain morbidities and mortalities.

(2) Production of extrarenal azotemia due to low blood pressure, resulting in a decrease in urea clearance and an increase in blood urea.

(3) Anoxemia due to poor absorption and transportation of oxygen. This may cause necrosis of tissue in vital organs, as in the brain, producing a temporary or fatal psychosis. In insufficiency of coronary circulation, even in younger individuals who have no coronary sclerosis, myocardial necrosis is produced, which is indistinguishable from myocardial infarction, yet no vessels are occluded. Such lethal lesions have been noted even in the younger group and it must, therefore, follow that it will more often occur in the older group. This, undoubtedly, is one of the explanations of the much higher death rate in the older sclerotic group; *i.e.*, they cannot tolerate a severe grade of anemia as well as the younger nonsclerotic patients.

If transfusions are given, undiluted fresh blood containing a normal concentration of prothrombin, red cells with normal intracellular potassium, normal white cells and platelets seems to be preferable to fresh citrated blood, or banked blood, especially in patients who are near exsanguination.

The rate at which blood is given to a massive gastric hemorrhage patient has received much attention. In the Knickerbocker Hospital group most of the transfusions have been given by our hematologist Dr. Rufus Stetson.<sup>32</sup> Amounts of 500 to 1,000 cc. have been administered by the direct method. In no case have we been able to associate a secondary hemorrhage with the amount or the rate of transfusion.

A conclusion must, therefore, be drawn that transfusion therapy should be used and that fresh blood by direct method is preferable.

*Mortality from Gastro-Intestinal Hemorrhage.*—In few other diseases are the statistics which appear in the literature quite so difficult to evaluate. Geographic distribution, what constitutes a massive gastric hemorrhage, the ratio of gastric ulcers to duodenal ulcers, and whether cases are selected at random, such as are admitted to a metropolitan hospital from a large ambulance district, or from a clinic where careful follow-up and dietary regimens are in vogue, are factors influencing the mortality and morbidity. Hence, a variation from one to 25 per cent is found in the reported series. Hinton,<sup>17</sup> reporting a series of 165 cases from the Fourth Division, Bellevue Hospital, has a nine per cent mortality. Chiesman<sup>11</sup> reports a 25 per cent mortality for patients having massive hemorrhage. Allen and Benedict<sup>3</sup> report 14.5 per cent in a series of 138 cases. Goldman<sup>16</sup> states: "The mortality of gross hemorrhage was 11.1 per cent from exsanguination alone, but rose to 15 per cent when the deaths from complications with hemorrhage were added. It should be emphasized in this connection that the additional 4.9 per cent mortality includes six patients in whom perforation ensued following the onset of hemorrhage, thus presenting two serious complications."

In 1935, Westermann<sup>37</sup> published a paper showing the appalling mortality from conservative treatment and suggested that some of these patients should be treated surgically. In the discussion of Westermann's paper, it was admitted that while he had achieved striking results, his colleagues still were inclined, in view of the operative risk, to favor conservative treatment. Since 1938, surgical treatment has had a constantly increasing number of advocates and the literature of 1939 and 1940 is replete with many articles by those who urge operative relief.

To acquire data and a cross-section surgical opinion on the subject of massive gastric hemorrhage, a questionnaire was sent to members of the New York, Western and American Surgical Associations. In all, 500 letters were sent. There were 248 replies and of these 107 furnished data. Permit me to thank the members of these associations for their courteous cooperation.

The answers indicate that 75 per cent of the surgeons strongly believe that surgery has a definite place in the treatment of massive gastric hemorrhage. The remainder are just as strongly convinced that it is entirely a medical

# MASSIVE GASTRIC HEMORRHAGE

TABLE I

112 PATIENTS OPERATED UPON DURING THE ACUTE BLEEDING PERIOD

## GASTRIC RESECTIONS (BOTH SEXES)

	AGE	NUMBER	DEATHS	% MORTALITY
GASTRIC ULCERS	ABOVE 45	23	6	26
	BELOW 45	11	2	18.1
	TOTAL	34	8	23.5
DUODENAL ULCERS	ABOVE 45	55	8	14.5
	BELOW 45	23	4	17.4
	TOTAL	78	12	15.4
TOTAL ALL RESECTIONS		112	20	17.8

TABLE II

548 PATIENTS TREATED CONSERVATIVELY

## CONSERVATIVE THERAPY

	SEX	AGE	NUMBER	DEATHS	% MORTALITY
GASTRIC ULCERS	M	ABOVE 45	75	22	29.3
		BELOW 45	48	9	18.7
		ALL	123	31	25.3
	F	ABOVE 45	19	5	26.3
		BELOW 45	8	0	0
		ALL	27	5	18.5
TOTAL		150	36	24	
DUODENAL ULCERS	M	ABOVE 45	164	36	21.9
		BELOW 45	179	11	6.14
		ALL	343	47	13.7
	F	ABOVE 45	35	8	22.8
		BELOW 45	20	1	5.0
		ALL	55	9	16.3
TOTAL		398	56	14.0	
TOTAL ALL ULCERS			548	92	16.7

TABLE III

HOSPITAL GROUPS TREATED CONSERVATIVELY WERE NOT COMPLETELY CLASSIFIED, AND ARE, THEREFORE, PLACED IN A SEPARATE GROUP

Hospital	G. U.*	D. U.†	M. U.‡	Mortality Per Cent
Barnes Hospital.....	18	60	0	7
Bellevue—Fourth Division.....	17	148	0	9
Clute, Howard M.....	4	20	6	33.3
New York Hospital.....	13	131	17	11
San Francisco Hospital.....	73	165	12	11.1
Strong Memorial Hospital.....	29	139	0	7.4
Toronto General Hospital.....	20	136	0	12
Totals.....	174	799	35	11.3

\* Gastric ulcer.

† Duodenal ulcer.

‡ Marginal ulcer.



problem and, if surgery is undertaken at all, it should be deferred until the patient has recovered from his exsanguination.

*Statistics of Conservatively Treated Cases.*—In the preparation of the statistical portion of this paper, 1,556 cases of peptic ulcer have been studied. Of this number, 112 were operated upon during the acute bleeding period (Table I). The remaining 1,444 were treated conservatively. This latter number is subdivided into three groups: 80 cases from the Knickerbocker Hospital (Table II), 448 from a questionnaire, and 1,008 designated as Hospital group (Table III). The Hospital group did not supply all the classifying data. A number of the conservatively treated group had interval operations, but as this is a separate problem, it is not discussed in this paper.

The mortality for the entire group of 1,556 cases is 17 per cent. The 1,008 cases in the Hospital group (Table III) have a mortality of 11.3 per cent; an apparent less rigid classification in this group. In the Knickerbocker and Questionnaire groups, massive gastric hemorrhage is interpreted as meaning a patient with 35 per cent hemoglobin or less, with a blood count of 2,000,000 red blood cells or less. Hence, moderate bleeding cases without mortality are eliminated. The 548 analyzed cases include 398 duodenal and 150 gastric ulcers, a ratio of approximately five to two. The mortality rate, however, of duodenal and gastric ulcers is reversed. It is approximately one to two, since gastric ulcer mortality is 24 per cent and duodenal mortality 14 per cent. There seems to be a general belief expressed in the literature that women withstand massive gastric hemorrhage better than men. In this analysis, there are 82 female patients with peptic ulcers, showing a mortality of 17.4 per cent as compared with 466 male patients with peptic ulcers having a mortality of 19.5 per cent (Table II).

It has long been recognized that the age of a patient is an important factor in the outcome of massive gastric hemorrhage. For purposes of analysis the age 45 was arbitrarily chosen as a dividing line.

The seriousness of bleeding in the upper age-group has been explained on the basis of arteriosclerosis. This, without doubt, is an important factor. However, in reading the histories of ulcer patients one is impressed with the length of time the average patient has had his symptoms. Furthermore, serious bleeding invariably is found in patients with chronic ulcers. In other words, serious bleeding usually takes place in old and chronic ulcers where arteritis and periarteritis is present. So, may it not be that in the older group, where the ulcer has actually existed longer, the local pathology is the deciding factor rather than the actual systemic arteriosclerosis.

Table II demonstrates that all cases of hemorrhage from peptic ulcer in those beyond age 45 is more serious than in the younger group. The mortality in 94 gastric ulcer patients above age 45 is 28.7 per cent as compared to a mortality of 20 per cent in 56 gastric ulcer patients below age 45. This is more noticeable in the duodenal ulcer group. One hundred and ninety-nine patients above age 45 had a mortality of 22 per cent as compared with 199 patients below age 45 who had only a 6 per cent mortality. The striking

difference in the mortality of these two groups does not justify too great an optimism for conservative treatment of the younger group, for it should be the responsibility of the diagnostician to recognize lethal bleeding in this group as well as in the older group.

A 20 per cent mortality in gastric ulcer patients below age 45 cannot be taken lightly. A death was reported in the Questionnaire group of a boy, age 14, and autopsy showed an easily resectable ulcer. The life expectancy of patients age 14 or 18 is equal to three or four times that of patients age 50 or 60.

The tables are inserted for detailed study of the various groups since they are more expressive than word analysis.

In the Knickerbocker series there were 456 patients admitted in the ten-year period from 1931 to 1940. Of these, 173 were ruptured ulcers. One hundred and eighty-two patients were admitted for bleeding, and of the bleeding group 80 were classified as massive gastric hemorrhage, of which 14 died, a mortality of 17.5 per cent. All of these massive bleeding cases were treated conservatively except four, which were operated upon for subtotal gastrectomy, one of whom died of pneumonia on the tenth postoperative day. All deaths occurred in the group above age 45 except three, one of whom had a gastric ulcer which at autopsy showed an open vessel in a sclerosed ulcer of the antrum.

There were 57 duodenal and 23 gastric ulcers, a ratio of five to two. In the Knickerbocker group there were 16 females, with four deaths, a mortality of 25 per cent. Of the four females who died, two were duodenal ulcers above age 45 and two were gastric ulcers below age 45. There were 64 male patients, ten of whom died, a mortality of 17 per cent. Of the ten males who died, one was a duodenal ulcer below age 45, four were duodenal ulcers above age 45, four were gastric ulcers above age 45 and one was a gastric ulcer below age 45. The divisions between gastric and duodenal ulcers in the sexes were approximately the same ratio, there being four females with gastric ulcers to 12 with duodenal ulcers, and 19 males with gastric ulcers to 45 with duodenal ulcers.

The mortality rate of the entire group shows seven gastric ulcer deaths and seven duodenal ulcer deaths, a mortality of 7.6 per cent, if computed for the entire 182 bleeding cases; or a mortality of 17.5 if computed on the 80 massive gastric hemorrhage cases. This group is included with the Questionnaire group in the statistical table.

*Operative Statistics.*—In the Knickerbocker and Questionnaire groups, 160 patients were operated upon during the bleeding period, many of them after prolonged bleeding (Table I). Of these, 112 had gastrectomies, either a Polya, a Billroth II, or some type of resection. Twenty of these patients died postoperatively, either from the operation or postoperative complications, such as pneumonia. This gives a mortality of 17.8 per cent for all types of ulcers.

TABLE IV  
GROUP OPERATED UPON BY VARIOUS PROCEDURES, SUCH AS LIGATION, PLICATION, LOCAL  
RESECTION, COAGULATION, *etc.*

48 Patients operated upon, without resection  
17 Deaths, a mortality of 35.4%  
Admittedly, most of these were less favor-  
able surgical risks

**ALPHABETICAL LIST OF CONTRIBUTORS OF CASES OF MASSIVE GASTRIC HEMOR-  
RHAGE, FROM WHICH THE DATA IN THIS PAPER IS COMPILED**

Contributors	No. of Cases Over Age 45	No. of Cases Under Age 45	Contributors	No. of Cases Over Age 45	No. of Cases Under Age 45
Abell, Irvin	1	1	Mason, James M.	2	1
Allen, Arthur W.	11		Masson, James C.	1	
Attix, Fred F.		1	Mastin, Edward V.	3	1
Barber, Robert F.	8	3	Meyer, Karl A.	1	3
Bates, Alfred K.	5	3	Miller, Edwin M.	1	
Benjamin, A. E.	3	4	Miller, Edwin L.	4	1
Best, R. Russell	9		Mills, William M.	1	
Black, Carl E.		1	Mixter, Charles E.	10	1
Bonn, Harry K.		1	Moore, Edward C.	1	2
Burdick, Carl G., and Hinton, J. Wm.	Bellevue Hospital —Fourth Division, 165 cases peptic ulcer reported		Moore, Robert M.	3	3
Carson, William J.		4	Morrison, Wayland A.	3	
Cave, Henry W.		1	Morton, Paul C.	1	1
Clute, Howard M.	30 cases reported in Hospital group		Morton, Lewis B.		1
Cole, Warren H.		1	Motzel, Albert J.		1
Cottam, Gilbert	1	1	Oughterson, Ashley W., and Harvey, Samuel C.	3	1
Dixon, Claude F.	1		Packard, George B., Jr.	1	6
Donovan, Edward J.	4	2	Patterson, Russel H.		2
Fudley, Guilford S.	1	4	Percy, Nelson M.	21	16
Dyas, Frederick G.	1		Peterson, F. R.	7	1
Eggers, Carl	1	2	Powell, Lester D.	1	2
Bloesser, Leo, and Klein, Russell	San Francisco Hos- pital, 250 cases pep- tic ulcer reported		Primrose, William A.	1	
Evans, John L.	4	1	Reichert, Frederick L.	1	1
Fahrni, Gordon S.		4	Wiggs, Theodore F.	4	2
Fairchild, Fred R.	1	1	Russell, Thomas H.	2	1
Fawcett, George G.	2	1	Sanders, Robert L.	4	1
Foster, John M., Jr.	1		Sauer, Paul K.	2	4
Foss, Harold L.	9	7	Schmidt, Edwin R.	9	5
Gallie, William E.		1	Schwyzer, Arnold	2	1
Garlock, John H.	2	3	Scott, W. J. Merle		Strong Memorial Hospital, 168 cases reported
Gillespie, M. G.	12	10	Seeger, Stanley J.	1	
Grace, Roderick V.		1	Smith, Joseph F.	1	
Graham, Everts A., and Kelly, Robert	Barnes Hospital, 78 cases reported		Smith, Morris K.	3	
Graham, Henry F.	8	10	Smithwick, Reginald H.	1	1
Graham, Roscoe R.	Toronto General Hospital, 156 cases reported		Smyth, Calvin M., Jr.	3	2
Hart, J. Deryl	3	6	Stone, Harvey E.	1	1
Hegner, Casper F.	2	4	Sturgeon, Charles T.	2	6
Hertzler, Arthur E.	1		Summey, Thomas J.	2	1
Heuer, George J., and Holman, Cranston W.	New York Hos- pital, 161 cases re- ported		Taylor, Alfred S.	1	
Heyd, Charles G.		1	Toland, Clarence G.	2	3
Holden, William B.	2		Truesdale, Philemon E.	10	9
Horsley, J. Shelton	5	2	Twyman, Elmer D.	4	
Hunt, Claude J.	2	1	Vaughan, George T.	1	
Hunt, Verne C.	9	3	Wallace, Hilen K.	4	2
Ide, Arthur W.	2	1	Westermann, John J.	5	3
Jackson, Arnold S.	6	4	Williams, Carrington	7	2
Joyce, Thomas M.	4		Wise, Walter D.	4	4
Larson, E. Eric	1		Wright, Arthur W., and Barber, W. Howard		Reported six cases having gastro- enterostomies who subsequently had massive gastric hemorrhage
Lee, Walter E.	11	7	Zinniger, Max M.	6	3
Lehman, Edwin P.	2	1	No name	1	1
Long, Le Roy D.	8	7	No name	1	
McDonald, A. L.	1		No name	1	1
MacFee, William F.	1		No name	1	5
Maes, Urban	Louisiana State University, 33 cases reported		No name	1	3

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There were 23 gastric ulcer patients above age 45, with six deaths, a mortality of 26 per cent. This compares favorably with the conservatively treated gastric ulcer cases. Ninety-four patients in the same age-group had 27 deaths, a mortality of 28.7 per cent.

In the group of duodenal ulcers above age 45, there were 55 operated upon, with eight deaths, a mortality of 14.5 per cent, as against the conservatively treated group of 199 patients with 44 deaths, a mortality of 22 per cent. Had these patients been operated upon in the 24- to 48-hour period, it is reasonable to assume the mortality would have been nearer that of interval gastrectomies, or near that of Finsterer<sup>15</sup> who performed 71 gastrectomies upon bleeding ulcer patients, with a mortality of 4.2 per cent.

The use of chemotherapy, given either preoperatively or as a massive dose intraperitoneally at the end of the operation, may still further reduce this mortality, especially since pneumonia seems to be a complication causing many of the deaths.

Forty-eight patients were treated by various operative procedures: gastro-enterostomies, pyloroplasties with excision of the ulcer, enterostomies or gastrostomies with ligation of the bleeding vessel or coagulation of the bleeding point. It is fair to presume that these patients were less favorable surgical risks, otherwise gastrectomies would have been undertaken. Of these 48 patients 17 died, a mortality of 35.4 per cent (Table IV).

### CONCLUSIONS

Analysis of this data justifies the following conclusions:

(1) Gastrectomy is the operation of choice, both for control of hemorrhage and for an ultimate cure. Bleeding following gastrectomy in surviving patients was not reported.

(2) Gastrectomy is often more difficult to accomplish in cases of duodenal than in cases of gastric ulcer.

(3) Local excision of a gastric ulcer combined with gastro-enterostomy apparently gives a satisfactory result.

(4) If the ligation of a vessel or plication of the ulcer only is accomplished, nonabsorbable suture material should be used. However, bleeding has recurred following this procedure.

(5) Gastro-enterostomy *per se* is of no value to stop immediate bleeding or to prevent recurrence.

(6) Vitamins, particularly B and C, given preferably by hypodermic in the postoperative period, will aid materially in an uneventful convalescence.

(7) Early operation before repeated exsanguination occurs, is essential for a lowered mortality.

### SUMMARIES OF CASES OF SPECIAL INTEREST

#### *Cases Reported in the Questionnaire Group*

Dr. William E. Gallie: *Recurrent Hemorrhage.*

Male, age 43, with a five-year history of gastric ulcer. Admitted to hospital with hematemesis and hemoglobin 80 per cent. Treated conservatively. Nine days later, a second profuse hemorrhage

occurred after which the hemoglobin was 43 per cent. In spite of transfusions, the hemoglobin fell to 32 per cent. A gastrectomy was then performed. Recovery uncomplicated, and the patient is now symptom free.

Dr. James C. Masson: *Lethal Hemorrhage without Demonstrable Lesion.*

A patient operated upon for repair of a postoperative interstitial hernia. At the same time, a vaginal hysterectomy for uterine prolapse and cystocele, and a perineorrhaphy for lacerated perineum was done. She had an uneventful convalescence. On the eleventh postoperative day, she passed a tarry stool. In spite of treatment, she died in a comparatively short time. Autopsy revealed the stomach to contain 1,500 cc. and the intestine 500 cc. of blood, but the source of bleeding could not be found.

Dr. E. Eric Larson: *Cauterization for Bleeding.*

(1) Male, age 58, was admitted for severe indigestion. Fifteen days later he had a very severe gastric hemorrhage. *Operation:* Duodenotomy, with cauterization of the pancreatic base of the ulcer. Pyloric occlusion with gastro-enterostomy was then performed. Patient recovered and has been well for the past two years. Roentgenograms show pylorus and gastro-enterostomy stoma both functioning.

(2) *Small Bleeding Ulcer; Difficult to Find.*

Male, age 38, died from massive gastric hemorrhage. When the stomach and duodenum were opened at autopsy, no bleeding point could be seen. Upon stroking the posterior wall with the hand, a fountain-like spray emitted through a pin-head-sized hole. Could the surgeon have found it?

Dr. Thomas H. Russell: *The Young Die Too.*

Boy, age 14, was admitted to the hospital for massive gastric hemorrhage. He was treated conservatively. Autopsy revealed a small ulcer on the anterior wall of the duodenum, which would have been easily resectable.

Dr. James M. Mason: *Recurrence of Bleeding.*

Male, age 64, was admitted for massive gastric hemorrhage. He was alcoholic and had cardiovascular-renal disease. Hemoglobin on admission was 35 per cent; R.B.C. 1,950,000. He was treated conservatively, followed by recovery. Readmitted nine months later for massive gastric hemorrhage. Hemoglobin 28 per cent; R.B.C. 2,000,000. Bleeding continued in spite of treatment. Autopsy revealed a duodenal ulcer with erosion of gastroduodenal artery.

Dr. Roderick V. Grace: *Bleeding Recurrent after Ligation.*

Male, age 35, was admitted for massive gastric hemorrhage. Duodenotomy was performed and a posterior duodenal ulcer, with a vessel in the center, was located. A gastrectomy was not feasible so the bleeding artery was ligated with chromic ligature. The ulcer was too fixed to admit its being plicated. Bleeding stopped, but on the fifth postoperative day the patient died of an apparent recurrent hemorrhage.

Dr. Albert J. Motzel: *Death from Pneumonia.*

Male, age 24, was admitted for massive gastric hemorrhage. He passed red blood by rectum, blood pressure not obtainable, pulse fast. After a 1,000 cc. blood transfusion his pressure was 70/50. In three days another severe hemorrhage occurred; pulse 120, R.B.C. 1,700,000. He received a large transfusion, with temporary recovery, but continued to bleed. Duodenotomy, under local anesthesia, on the seventh day disclosed a posterior duodenal ulcer with bleeding artery, which was ligated with silk. Patient improved and four days later R.B.C. 4,240,000, 12.3 Gm. hemoglobin. On the fifth postoperative day, he developed pneumonia, and in spite of chemotherapy succumbed on the twenty-ninth postoperative day.

Dr. Reginald H. Smithwick: *Extent of Operation Possible.*

Male, age 30, had had repeated hemorrhages during a period of three weeks. R.B.C. 1,500,000. At operation, an ulcer was found on the lesser curvature, posterior wall, involving the gastric artery. The crater was 3 cm. in diameter, and the ulcer proved to be cancerous. Practically a total gastrectomy was performed, with recovery.

Dr. Irvin Abell: *Perforation and Bleeding Ulcer.*

Male, age 42. Past history of typhoid. Had recurrent attacks of excruciating pain in abdomen over a period of 12 years. On admission, stools had been tarry for past 24 hours. He was given two blood transfusions totaling 915 cc. Bleeding continued and hemoglobin reached 30 per cent, R.B.C. 1,860,000. After the transfusions a celiotomy demonstrated a perforated gastric ulcer partially concealed by the liver, colon and omentum. Pólya type of gastrectomy was performed, also appendectomy, resulting in a cure.

Dr. Edwin M. Miller: *Massive Transfusion.*

Male, age 64, was admitted for massive gastric hemorrhage. At noon he was *in extremis*. A continuous blood transfusion was then started and at four o'clock his condition was thought to be operable. The stomach was dilated and solidly filled with a massive blood clot, which could only be



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removed by scooping it out by hand. After removal of the clot, it was possible to see a pumping gastric artery in the center of a saddling ulcer on the lesser curvature. A Billroth II resection, with an anterior gastro-enterostomy and an entero-enterostomy were performed. One year postoperative the patient is in excellent health.

Dr. John M. Foster, Jr.: *Surgery Successful Even After Long Delay.*

Male, age 48, with chronic ulcer. Admitted after four days of profuse bleeding. R.B.C. 1,250,000. Improved with conservative treatment, but on ninth day after admission he again had moderate hematemesis. On the eighteenth and nineteenth days, he vomited copious amounts of blood. A posterior duodenal ulcer was found, with an artery that spurted ten inches. The ulcer could not be removed on account of the induration. A posterior Pólya, with exclusion of the ulcer was performed. "Upon being brought to the operating room both arms were placed on arm-boards and with four available donors we transfused him in both arms. The amount of blood received during surgery was about 1,200 cc. He left the table with a much better color and a distinct slowing of the pulse." Convalescence was complicated by pneumonia. To date he is in excellent condition without symptoms.

Dr. William F. MacFee: *Successful Subtotal Gastrectomy.*

Male, age 61, had had intermittent, exsanguinating hemorrhages for three weeks, of such severity and frequency that operation became imperative. A subtotal gastrectomy was, therefore, performed, with cure of the patient.

Dr. Claude F. Dixon: *Reactivation with Bleeding of an Apparently Healed Duodenal Ulcer.*

A gastro-enterostomy gave relief for 16½ years. He was readmitted for a large tumor in his upper abdomen suspected of being a carcinoma. Exploration revealed a gastrojejunalcolic fistula. Jejunostomy was performed at this operation for feeding purpose. The mass rapidly disappeared. The abdomen was reopened four weeks later, and as the duodenal ulcer had practically disappeared, the gastro-enterostomy was disconnected; the marginal ulcer excised and normal continuity reestablished. A double-barrel colostomy was then made at the site of the colon fistula. Progress was excellent for three weeks, when a terrific hemorrhage occurred. He was given 16 transfusions, two being of 1,500 cc., three of 1,000 cc., and 11 of 500 cc. He was never transfused except as a last resort. Autopsy revealed a reactivation of the duodenal ulcer, with erosion of the pancreaticoduodenal artery.

Dr. Walter D. Wise: *Bleeding after Exclusion Operation.*

Female, age 34, suffering from recurrent hemorrhages. She was explored and such an extensive duodenal ulcer was found that resection was considered impossible. A gastro-enterostomy was performed. She subsequently bled again. A second exploratory was done at which time resection was again considered too formidable, so a Divine exclusion operation was performed. This gave the patient relief for about five years. She recently had another attack of bleeding.

Dr. Guilford S. Dudley (*Second Surgical Division—Bellevue*): *Duodenal Fistula.*

Male, age 74, was admitted with perforated prepyloric ulcer, for which he was successfully operated upon. On the twenty-second postoperative day, he had a severe gastric hemorrhage, followed by shock. Supportive treatment with 500 cc. transfusion caused improvement. In 24 hours, he had a second severe hemorrhage, with marked shock, blood pressure 96/66, pulse 130. Continuous transfusion and operation followed. There was a large posterior duodenal ulcer penetrating into the pancreas, with an open vessel. Subtotal gastrectomy with resection of the ulcer and ligation of the bleeding vessel was accomplished. Difficulty was encountered in closure of the duodenal stump; cigarette drain down to the duodenal stump and wound closed. Duodenal fistula developed on fourth postoperative day, with drainage of blood and bile. Patient developed pneumonia and died on thirteenth postoperative day.

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## SURGERY IN PEPTIC ULCERATION OF STOMACH AND DUODENUM IN INFANTS AND CHILDREN\*

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BECAUSE of the general impression that peptic ulceration of the stomach and duodenum is excessively rare in infants and children, there is a tendency to neglect this lesion in young patients. For this reason, it seems to us of interest to present evidence which, though largely indirect, indicates that the disease is not very uncommon.

Several internists and roentgenologists (*e.g.*, Nisbet, 1911; Michaëlsson, 1925; Dickey, 1926; Potter, 1930; Jankelson, 1932; Reuben, 1934; Hirsch, 1935; Prévôt, 1935; Blechmann, Gutmann and Nemours-Auguste, 1932) have published two or more cases in which the diagnosis of peptic ulcer was adequately established on clinical grounds, and others (Wertheimer, 1882; Adler, 1907; Loeber, 1929; Herz, 1930; Oldfield, 1932; Bermond, 1933; Moore, 1934; Gillespie and Gianturco, 1935; Menna, 1937; Cathala, 1938) have reported individual examples in this category. Many of these authors voice the opinion that the disease is not rare but frequently overlooked. Altogether, a considerable number of ulcers, about 200 or 300 in the world literature, have been demonstrated at autopsy,<sup>†</sup> and undoubtedly many have existed undiagnosed in patients who have recovered or who have died without postmortem examination.

By careful search, we have gathered what we believe to be an almost complete collection of the cases reported in which operations have been performed for peptic ulcers in infants and children. The cases number 119, and include one of our own. The diagnoses, we think, though based on clinical features

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\* This paper is not concerned with peptic ulceration of the esophagus or of Meckel's diverticulum. For those who are interested in these subjects, the articles by Diamantopoulos (1926), and Black and Benjamin (1936) should be consulted.

† Through the kindness of Dr. B. Earl Clarke, pathologist at the Rhode Island Hospital, we record, here, a previously unpublished case of an acute ulcer of the posterior wall of the duodenum, 3 Mm. in diameter, observed at autopsy in a male, aged two months. The infant was well until two or three days before death. It then refused food and whined as if in pain. There was no vomiting, and blood was not noticed in the stools. Except for a moderately enlarged heart with a patent foramen ovale and a wide inter-ventricular defect, nothing else abnormal was observed at the postmortem examination. A blood culture was not made.

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or gross observations at operation in some of the patients in whom gastroenterostomy alone was performed, can scarcely be questioned. We have also accumulated representative reports of 124 cases in which no operation was undertaken. In most of these instances, the diagnoses were established at autopsy, and in the others the clinical features, often substantiated by characteristic roentgenologic findings, were unmistakable.

An analysis of our collected cases shows that ulcers in the newborn, by which we mean infants in whom the symptoms become outstanding within the first two weeks of life, have special characteristics: (1) The great majority, at least of ulcers that are recognized, bleed seriously, or perforate, or do both (Table I); (2) in many the onset is precipitous without recognizable premonitory symptoms or signs; (3) except in a few cases, neither clinically nor at autopsy, is there evidence of intracranial injury, or localized or generalized sepsis; (4) with few exceptions the lesions are acute, without cellular reaction or bacterial invasion; (5) because of the sudden, acute, fulminating symptoms, very few of these newborn patients are operated upon; (6) duodenal ulcers outnumber the gastric in a ratio of 2:1 (Table II); and (7) males outnumber females, but not strikingly so (Table III).\*

Peptic ulcers have been shown to occur even *in utero* (Lee and Wells, 1923).

TABLE I  
TYPES OF ULCER REPORTED IN VARIOUS AGE-GROUPS

	Stenosing	Perforated	Bleeding	Persistently Painful, etc.	Totals
Newborn (0-14 days).....	1	18	22	1	42
15 days-1 year.....	8	15	25	6	54
2-6.....	2	3	10	5	20
7-11.....	18	15	8	16	57
12-15.....	31	26	3	12	72
Totals.....	60	77	68	40	245

Note that: (1) At least among the cases which have been recognized, ulcers in the newborn, and in the early months of life, characteristically, either bleed seriously or perforate, or do both.

(2) The number of cases of all types, which are recognized, is small in children between two and six years of age.

(3) Among the recognized cases the incidence of pyloric stenosis and perforation increases during the later years of childhood, while the occurrence of serious hemorrhage decreases.

(4) After the eighth year, there are a considerable number of patients with uncontrollable abdominal symptoms, especially pain.

During the first 24 months of life, beyond the newborn period, the number of infants with ulcer diminishes. The nature of the disease also changes, as follows: (1) Although again the great majority of ulcers bleed grossly, or perforate (Table I), there are often premonitory symptoms such as refusal of feedings, evident abdominal pain, vomiting, occasional streaking of blood in the vomitus and melena, sometimes occurring over a period of weeks or

\* Kennedy (1926), and others, believe that most cases of melena neonatorum are due to ulcers, and that many of them heal. He states (1924) that acute ulcers are often overlooked at autopsy, and that, frequently, they are quite invisible in a fresh specimen although they may be seen easily if the specimen is examined after a few hours of fixation.



months before the onset of graver symptoms; (2) persistent pylorospasm or inflammatory or cicatricial pyloric stenosis is seen occasionally; (3) many of the patients are septic and marasmic, and the ulcers when seen at autopsy present, as a rule, an acute, subacute or chronic inflammatory base in which are seen numerous bacteria; (4) because of poor general condition very few of these patients are operated upon; (5) in an undetermined number, the symptoms recede and health is regained; (6) in this group the duodenal and pyloric ulcers outnumber the gastric in a ratio of more than 5:1 (Table II); and (7) males outnumber females (Table III).

TABLE II  
RATIO OF DUODENAL AND PYLORIC TO GASTRIC ULCERS IN VARIOUS AGE-GROUPS

	Duodenal and Pyloric	Gastric	Total
Newborn (0-14 days).....	26 (2)*	12 (1)	38
15 days-1 year.....	43 (5)	8 (1)	51
2-6.....	16	6	22
7-11.....	44	16	60
12-15.....	55	17	72
Totals.....	184 (3)	59 (1)	243

\* Ratios are in parentheses.

Note that: (1) The ratio of duodenal and pyloric to gastric ulcers is approximately 2:1 in the newborn.

(2) This ratio is about 3:1 for the entire group.

Between the ages of two and six years, the recognized examples of the disorder are very few (Table III). Among 243 cases, only 22 occurred within this period. This contrasts strongly with 89 recorded for the first 24 months of life, 60, for ages between seven and 11 years, and 72 for ages between 12 and 15. Among the examples reported, chronicity, hemorrhage, perforation and stenosis are outstanding features and, except in the children with burns, foci of infection are observed only rarely.

TABLE III  
AGE AND SEX DISTRIBUTION AMONG 243 CASES OF  
DUODENAL AND GASTRIC ULCER

	Male	Female	Sex Not Stated	Total
Newborn (0-14 days).....	15	11	12	38
15 days-1 year.....	22	15	14	51
2-6.....	11	9	2	22
7-11.....	35	22	3	60
12-15.....	43	23	6	72
Totals.....	126	80	37	243

Note that in all age-groups, males outnumber females, but not strikingly so.  
The ratio of males to females for the total number is approximately 1.5:1.

As age advances beyond the seventh year, there is a rise in the number of cases recognized, with special accentuation of the symptoms of pyloric stenosis and perforation (Table I). Hemorrhage recedes into the background. A few of the children require surgical treatment because of persistent, uncontrollable indigestion.

Over 70 per cent of the patients reported between the ages of seven and 15 were operated upon. On this basis there must be a large number of unrecognized or unreported cases of acute or subacute ulcer at this time of life, for it is scarcely possible that such a high proportion of the ulcers of childhood should lead to complications which require surgical intervention. It seems probable that acute and subacute ulcers masquerade under diagnoses such as chronic appendicitis, intestinal tuberculosis, mesenteric lymphadenitis, vermiculosis, allergic indigestion, or neurosis.

Among the cases reported in this age-group (seven to 15), the symptoms have often been present intermittently or continuously over a period of months or years. Chvostek (1882) noted a male, age 18, who had had indigestion since age four. Autopsy showed two large, round gastric ulcers, one at the cardia and one at the pylorus, the latter of which had caused pyloric obstruction. Parmentier and Lasnier (1908) told of a female, age 20, whose symptoms of ulcer had been present since infancy; she was improved on medical treatment. Pepper (1899) observed an autopsy on a patient, age 20, whose epigastric symptoms dated back to early childhood and in whom death was due to cicatricial pyloric stenosis. Among patients who were operated upon after the age of 15, and who, thus, were not included in our collection, Ettman (1936) recorded the story of a girl, age 16, whose symptoms for the preceding 18 months were characteristic of ulcer and who then perforated the duodenum; Schalij (1923-1924) reported upon a female, age 18, with recurrent epigastric distress since the age of 12, and high gastric acidity, who at operation revealed a callous ulcer of the duodenum; and Bignami (1939) described a girl, age 17, who had been treated for abdominal distress since the age of 11, and whose chronic duodenal ulcer was relieved by gastro-enterostomy. Von Cackovic (1912) and Proctor (1925) noted that in a considerable number of cases of ulcer in adults the symptoms date back to childhood. Several authors (Kalk, 1928; Rogers, 1928; Hirsch, 1935; Meltzer and Graf, 1936; and Bloch and Serby, 1937) stress the frequency of a familial history of ulcer in affected children.

*Surgical Considerations.*—Because of advances made in management during the preoperative, operative and postoperative periods, operations upon children, generally speaking, are safer than they were formerly. No rule of thumb can be made in regard to infants and children who present gross gastro-intestinal hemorrhage, or in those in whom septic or marasmic conditions such as malnutrition, furunculosis, otitis media and burns, complicate the picture, but for otherwise healthy children with chronic hemorrhage, perforation, pyloric occlusion, or those in whom pain persists after adequate medical treatment, operation may be said to be indicated.

Our interest in surgery of peptic ulcer in infancy and childhood was aroused by the following case:

**Case Report.**—Perforated Duodenal Ulcer—Sutured 34½ hours after birth. Recovery. F. W. F., colored, normal appearing, full-term, male infant, weighing seven

pounds and one ounce, was born in the Louisville City Hospital February 19, 1934, at 11:03 A.M.

The mother, age 25, had given birth to four full-term infants in the hospital previously. The third one had died one week after a Ramstedt operation for pyloric stenosis; there was no autopsy. There had been one miscarriage at the third month, but the history did not suggest tuberculosis or syphilis, and the mother's blood Wassermann reaction had been negative on all admissions. When seen in the Prenatal Clinic during the eighth month the blood Wassermann reaction was again negative. Labor began at 2 A.M., February 19, 1934, and she was admitted to the hospital four hours later. The membranes ruptured at 10:45 A.M. During the second stage, which lasted 18 minutes, chloroform was administered in small amounts, and the birth was completed spontaneously in the left occiput anterior position.

There was no asphyxia and the infant cried immediately. He was put to the breast at 6 P.M. and at 10 P.M., and took 35 cc. of water during the first 12 hours. On the day of birth he had one normal meconium stool and voided once. On the next day he was placed on the breast every four hours and allowed water in 15 to 20 cc. amounts between feedings. Another meconium stool was passed and he voided twice. When he was fed at 2 P.M., 27 hours after birth, nothing abnormal was noted, but he cried a great deal shortly afterward, and at 4:30 P.M., 29½ hours after birth, the nurse observed that the scrotum was swollen and that the abdomen was distended. He had not vomited. The rectal temperature was 99.8° F. He was given a colonic irrigation, upon which a pasty, brown stool and a little gas were expelled.

When seen at 6:30 P.M., the abdomen was moderately distended, and the scrotum was ballooned so that the skin seemed stretched to the thinness of paper. The scrotal sac was symmetrical, transilluminated readily, and was tympanitic on percussion. The scrotum could be reduced in size by compression, but on release it refilled and, if at the same time pressure was exerted on the abdomen, the scrotum would distend with a swishing sound. Rectal examination showed nothing abnormal.

Roentgenograms were made with the infant upright, and again in an inverted position. They showed a very large amount of free air in the peritoneal cavity and in hernial sacs, which extended into the scrotum. The findings were diagnostic of a perforation in the gastro-intestinal tract, although the exact nature of the lesion was not suspected preoperatively.

Abdominal exploration was performed under chloroform anesthesia at 9:30 P.M., 34½ hours after birth. This procedure was carried out by Dr. Jacob M. Mayer, then resident surgeon. On opening the peritoneal cavity, free gas and a small amount of serosanguineous fluid were observed. There was moderate hyperemia of the serous surfaces and, here and there, loops of small bowel were bound together by fresh fibrin. The tip of a finger could be introduced into both sides of the scrotum, but no bowel or omentum was present in either hernial sac. Investigation of the upper abdomen revealed an exudate in the region of the gallbladder and duodenum, where all the structures were matted together. When the fresh adhesions were separated, a perforation was found on the anterosuperior surface of the duodenum, immediately distal to the pyloric vein. A moderate amount of bile and mucus exuded from it. The perforation was oval in shape and about 3 Mm. in greatest diameter. There was no induration or edema of its borders and the opening appeared as though a bite had been taken out of the normal duodenum by a sharp instrument. The defect was closed transversely with a row of fine, interrupted chromic catgut sutures and was reinforced by a tier of "A" silk sutures over which was drawn a portion of the gastrocolic omentum. The abdomen was closed securely in layers without drainage. In applying the dressing, the wound was isolated from the umbilicus.

The infant was returned to the ward in excellent condition and was given 80 cc. of 10 per cent dextrose solution intravenously and 350 cc. of isotonic sodium chloride

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subcutaneously. During the following 11 hours he vomited small amounts of brownish fluid on three occasions.

At 11 A.M. the next morning, 15 mg. of phenobarbital in a small amount of water were administered by mouth, for restlessness. After 3 P.M., he took water by mouth in 15 cc. amounts at one and one-half hour intervals. At 6:15 P.M., he vomited again and gastric lavage evacuated a moderate amount of brownish fluid. The abdomen was not distended and the rectal temperature had not risen above 99.8° F. He was given 100 cc. of 10 per cent dextrose intravenously and 125 cc. of Hartmann's Ringer-lactate solution subcutaneously. By this time cultures of the free peritoneal fluid, taken at the time of operation, showed no growth.

On February 22, the second postoperative day, the rectal temperature rose at 8 A.M. to 102.2° F. At 9 A.M., he was given 10 cc. of breast milk with 10 cc. of water; at noon and at 3 P.M., he was fed 15 cc. of breast milk with 10 cc. of water and at 6 P.M. and 10 P.M., 20 cc. of breast milk with 10 cc. of water. Water was also given, 30 cc. at a time, during the day, half-way between feedings, and 125 cc. of Hartmann's solution were administered subcutaneously.

On February 23, the third postoperative day, he was fed, as on the last previous occasions, at 2 A.M., and 6 A.M., and was then put to the breast every three hours; each feeding was supplemented by 30 cc. of breast milk. The rectal temperature on this day remained below 99.6° F., and the abdomen was soft.

On February 24, the fourth postoperative day, the temperature was normal and remained so throughout the rest of the stay in the hospital. He took the breast fairly well, although it was necessary to continue the supplementary feedings. The weight, which had dropped seven ounces on the second postoperative day, again approached the birth weight. On the ninth postoperative day he weighed eight pounds, but gradually lost again to seven pounds and two ounces on March 10, then gained gradually. The wound healed cleanly. There was no apparent infection at the umbilicus at any time.

On March 9, the seventeenth postoperative day, a gastro-intestinal examination showed 25 per cent retention of barium in the stomach at six hours; there was a slight residue in the stomach after 24 hours. The infant was discharged in excellent condition March 17, 1934, 26 days after operation. His weight on this date was seven pounds and nine ounces.

The barium meal was repeated on March 31, 40 days after operation. Sixty per cent was found in the stomach at the end of six hours. Five hours later, there was still a large amount of barium in the stomach, but some of it was scattered through the intestinal tract. At 24 hours, the infant had not vomited, and the stomach and most of the bowel were empty.

The patient was readmitted for observation November 2, 1934, at the age of eight and one-half months. According to the mother he had been well since discharge. He had never vomited and the bowels had moved without medication. He had eaten cereals and vegetables in addition to breast milk, orange juice and cod liver oil. He was found to be well-developed, and weighed 17 pounds. The abdominal wound was solidly healed. He had an umbilical hernia. Both inguinal rings were enlarged but definite herniae could not be demonstrated. The testicles were palpable in their normal positions. On November 5, the gastro-intestinal examination was repeated. At the end of six hours there was slight retention of barium, and four hours later the stomach was empty. On November 11, a gastric analysis, using for stimulation 60 cc. of 7 per cent alcohol with histamine added, gave clear, mucoid specimens which contained no blood; the fasting specimen showed free hydrochloric acid 32, total 58; at one-half hour, free 18 and total 24; at one hour, free five and total nine.

On April 30, 1935, 14 months after operation, the child was returned for further observation. He had been well, and his development had proceeded satisfactorily. On May 3, a barium meal revealed the stomach and duodenum to be normal in size, shape, position and function. Barium passed freely from the pyloric antrum into the duodenum and

there was no six-hour residue. The gastric analysis was repeated, this time using 50 cc. of 7 per cent alcohol and 0.09 cc. of 1:1,000 histamine solution. No free hydrochloric acid was found in any of the specimens; the total acidity in the fasting contents was 18, at one-half hour 50, and at one hour 45. Possibly, it is of significance that on the day this determination was made, the rectal temperature was 101.2° F.; two days later he was transferred to the isolation ward with a well-developed case of measles. Recovery was complicated by acute catarrhal otitis media.

The child was studied again in February, 1940, at the age of six. He was in good health. Gastro-intestinal examination showed the esophagus and stomach normal and empty at six hours. There was a smooth outpouching from the duodenal bulb which gave the appearance of a small diverticulum. At 24 hours, the entire tract was empty of barium except for the lower colon. Gastric analysis showed for the fasting specimen free hydrochloric acid two, total 150; one hour after 60 cc. of 7 per cent alcohol, free 20, total 130.

TABLE IV  
SITUATION OF ULCERS, AND INDICATIONS FOR OPERATION

	Pyloric Obstruction	Perforation	Hemorrhage	Persistent Pain, etc.	Totals
Stomach.....	7	21	1	1	30
Pylorus or duodenum.....	42	21	10	10	83
Pylorus and duodenum.....	4	..	..	..	4
Stomach and duodenum.....	..	1	..	..	1
Accessory pouch of anomalous stomach...	..	..	1	..	1
Totals.....	53	43	12	11	119

Note that: (1) The pyloric and duodenal lesions constitute 72 per cent of those operated upon.

(2) The indications for operation are, for the most part, pyloric obstruction, perforation of the duodenum or stomach, hemorrhage from the duodenum, or persistent pain due to a pyloric or duodenal ulcer.

Among the 119 cases of peptic ulcer of the stomach or duodenum operated upon between the ages of 34½ hours and 15 years, 53 were for pyloric stenosis, 43 for perforation, 12 for hemorrhage and 11 for uncontrollable symptoms (Table IV). The stomach was involved in 30 cases, the pylorus or duodenum in 83, while in five other cases there were multiple lesions involving more than one part, and in one there was an ulcer in an accessory pouch of an anomalous stomach.

TABLE V  
INDICATIONS FOR OPERATION, AND NUMBER OF PATIENTS OPERATED UPON, IN VARIOUS AGE-GROUPS

	Pyloric Obstruction	Perforation	Hemorrhage	Persistent Pain, etc.	Number of Patients Operated Upon
Newborn (0-14 days).....	1	5	..	..	6
15 days-1 year.....	3	3	3	..	9
2-6.....	1	3	4	..	8
7-11.....	18	7	2	4	31
12-15.....	30	25	3	7	65
Totals.....	53	43	12	11	119

Note that: (1) Most of the operations have been upon older children.

(2) The largest number of procedures have been carried out for pyloric obstruction and for perforation, a smaller number for hemorrhage and persistent symptoms.

The indications for operation and the number of patients operated upon in the various age-groups are shown in Table V. In the very young, the



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indications were: Persistent pylorospasm, pyloric stenosis, perforation or hemorrhage; in the small group between the ages of two and six years, hemorrhage or perforation; and in the larger groups between seven and 15 years, predominantly cicatricial or inflammatory pyloric stenosis, acute perforation or, in a few, uncontrollable pain. Most of the operations were performed in later childhood.

TABLE VI  
TYPES OF OPERATION, AND MORTALITY RATES\*

	Closure of Perforation	Pyloroplasty or Gastro- enterostomy	Resection	Totals	Mortality Rate (Per Cent)
Newborn (0-14 days).....	5 (4)	..	..	5 (4)	80.0
15 days-1 year.....	2 (1)	2 (1)	1 (1)	5 (3)	60.0
2-6.....	1	2	1	4	0.0
7-11.....	5 (1)	21 (1)	4	30 (2)	6.7
12-15.....	24† (2)	30	11 (1)	65 (3)	4.6
Totals.....	37 (8)	55 (2)	17 (2)	109 (12)	11.0

Parentheses indicate deaths.

Note that the mortality rate in the very young has been high, while the rate in the older children has been quite low.

\* The following cases are not included in this table:

Sanjck, Weber, Becker; result not stated.

Michaëlsson; gastro-enterostomy, resection elsewhere, at age 21, for jejunal ulcer; result not stated.

Michaëlsson; gastro-enterostomy, second operation at age 17, for jejunal ulcer; died.

Bufe, John; appendicectomies in patients with bleeding ulcers; died.

Lee and Wells; lysis of adhesions in newborn infant with perforating gastric ulcer; died.

Berglund; exploratory celiotomy in an infant with bleeding duodenal ulcer; died.

Phélip and Fey; operative perforation of small bowel in infant with perforated gastric ulcer; died.

Shore; exploratory celiotomy in infant with perforated gastric ulcer; died during operation.

von Möriz; exploratory celiotomy in child with perforated duodenal ulcer and peritoneal abscess; died.

Bechtold; drainage of abdomen, only, in child with perforated gastric ulcer; died.

Peutz; exploratory celiotomy for bleeding duodenal ulcer; recovered.

† The case of Andersen is included in this table, both under closure of perforation and under gastro-enterostomy, and the case of Angel and Angel, and two of Deuticke are included, both under closure of perforation and under resection. In each case there was a long interval between the first and second operations.

The procedures (Table VI) are grouped under the headings: Closure of perforation; gastro-enterostomy (including pyloroplasty); and resection. Although closure of a perforation was carried out in five newborn infants, only our own recovered. The next youngest survivor was a male, age three months, reported by Selinger (1930)—with a recent perforation of the stomach which had sealed over. Downes (1923) successfully sutured an acute perforation of the duodenum in a child, age three. Between the ages of seven and 11 years, five perforations were closed with only one death—in a very ill child, age nine, whose perforation occurred nine days before operation. In the age-group between 12 and 15, 24 perforations were closed with only two deaths, one in a child, age 14, who was operated upon after a delay of 21 hours, and the other, in a boy, age 15, who died 17 days after operation because of an apparently unrelated intestinal obstruction.

The 52 gastro-enterostomies and three pyloroplasties, which are here grouped together, were accomplished with only two fatalities, one in a male infant, age two months, upon whom a Ramstedt pyloroplasty was performed,

under a mistaken diagnosis, and who died of hemorrhage from a duodenal ulcer, and the other, in a boy, age 11, who died following drainage of an hepatic abscess two months after gastro-enterostomy for pyloric stenosis.

We feel the record of resections of stomach and duodenum is remarkable. There were 17 in all, with only two fatalities, one following a pyloroduodenectomy for a large, deeply penetrating juxtapyloric ulcer (Landivar, 1928), and the other, in an infant, age 22 months, with a stenosing ulcer 1 cm. above the pylorus. The surgeon in the latter case (Stohr, 1925) stated that, in his opinion, a gastro-enterostomy would have sufficed.

In Table VI, the mortality rates at different ages may be seen. The chief points of interest are that the rate in the very young has been high (70 per cent), and for the adolescent child rather low (4.6 per cent).

Table VII is introduced for those who may use this article for reference. It indicates the names of the authors; the types of operations performed in the various age-groups; and the survival or death of the patient as the case may be.

Ladd's case has not been published previously. A boy, age 11, gave a history of vomiting and loss of weight of two years' duration. Roentgenologic examination showed pyloric obstruction with 50 per cent gastric retention at the end of 18 hours. A posterior gastrojejunostomy was performed in June, 1938, for an indurated pyloric ulcer. In April, 1940, the boy had gained 33 pounds in weight and was having no symptoms.

Imbassahy refers to the case of E. Mensi, the report of which we have been unable to obtain in the original (*Policlinica infantile*, January, 1935). A girl, age 13, had had attacks of headache, obstipation and vomiting. Roentgenologic studies showed a niche, characteristic of ulcer, in the duodenal bulb. She was cured by a gastro-enterostomy.

The fact should be mentioned that children are no more immune from the dangers of postoperative gastrojejunal ulcer than are adults. This is seen from the report of three cases by Michaëlsson (1925). We have found two other cases of postoperative jejunal ulcer in individuals within the age-groups under discussion. One of these was described by Freund (1903), and also by Tiegel (1904), the other by Strode (1933).

#### SUMMARY AND CONCLUSIONS

Our rather complete examination of the literature on the subject forces us to conclude that there are a considerable number of infants and children who at one time or another have peptic ulcers of the stomach or duodenum. We believe that at ages up to and including adolescence there are a large number of unrecognized or unreported ulcers of a potentially serious nature. Probably many of the lesions are acute and superficial and heal quite rapidly when the regimen is altered in some simple manner. In a few cases, the symptoms persist and, if a study with barium is undertaken, an ulcer is found which often shows a definite crater. Roentgenologic studies should, we think, be made more often in the younger patients.

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TABLE VII  
OPERATIONS FOR PEPTIC ULCER OF THE STOMACH AND DUODENUM IN INFANTS AND CHILDREN

	Closure of Perforation	Pyloroplasty	Gastro-enterostomy	Resection	Appendicectomy	Exploration Only	Newborn <sup>1</sup> (0-14 days)
Newborn (0-14 days)	Dunham; Theilander and Mathes; Smythe; Bird, <i>et al.</i> *						
15 days-1 year	Stern, <i>et al.</i> Selinger <sup>†</sup> ; Rosset	Palmer <sup>‡</sup> ; Bode		Stohr		Peutz; Berglund; Shore; Pheip and Fey von Möriz	15 days-1 year
2			Alsherg; Nettelblad				2
3	Downes				Bute		3
4						Bechold	4
5					John		5
6							6
7	Norlin; Tashiro and Kobayashi						7
8		Bloch, <i>et al.</i> ‡	Nesselrode, <i>et al.</i> ; Miller Lund; Roeder; Ceballos				8
9	Lilienfeld-Toul; Lohr <sup>†</sup>		Bona; Carro <sup>1</sup>		Paus		9
10	Karstad <sup>‡</sup>		Carriek; Smyth, <i>et al.</i> ; Toro; Gudiatis		Strode <sup>1</sup>		10
11			Toro; Norenberg; Vasconcellos; Kennedy; Thevenard; Michaelsson <sup>1</sup> ; Quarella; Henderson; Reydermann; Ladd	Oliver; Pototschniz			11
12	Anzel and Anzel <sup>1</sup> ; Karstad <sup>‡</sup> ; Deuticke <sup>6</sup> ; Paterson; Gordon;		Toro; Larret, <i>et al.</i> ; Weber; Pedraza (Solier) <sup>1</sup> ; Rodin; Onazo and Daza; Norenberg; Micheli; Clairmont; Sanjck <sup>10</sup>	Rodin; Landivar; Deuticke <sup>6</sup> ; Bertrand, <i>et al.</i> ; Anzel and Anzel <sup>1</sup>			12
13	Andersen <sup>5</sup> ; Cheyne and Wilhe; Nordentoft <sup>†</sup> ; Theile (de Quervain); López		Posner <sup>1</sup> ; Kellogg <sup>4</sup> ; Mensi; Andersen <sup>5</sup> ; Proctor; von Cackovic; Caldwell; Micheli	Diekey; Deuticke <sup>6</sup>			13
14	O'Flynn; Selvaag <sup>3</sup> ; Roeder; Wetterstrand; Holm; Korteweg		Paus; von Cackovic; Lohr; Reydermann; Proctor <sup>1</sup>	Stocker; Michaelsson <sup>11</sup>			14
15	Miklos <sup>3</sup> ; Imfeld; Holm; Ricard		White <sup>4</sup> ; Nordentoft (Harsloff); Cavina; Theile (Schanzlin); Micheli; Michaelsson <sup>12</sup> ; Weber <sup>10</sup> ; von Cackovic; Dienstfertie	Abadie; Iwata; Becker <sup>10</sup>			15

\* Recovery of patient is indicated whenever name of author is underlined.  
† Key: 1—Plus pyloric exclusion.  
2—Plus cauterization of ulcer.  
3—Plus cauterization.  
4—Plus excision of ulcer.  
5—Gastro-enterostomy; later, two operations for closure of perforations.

6—Closure; later, a resection.  
7—Plus gastro-enterostomy.  
8—Gastro-duodenostomy.  
9—Gastro-enterostomy done later.  
10—Result not stated.

11—Previous gastro-enterostomy.  
12—Operation elsewhere for jejunal ulcer at later date; result not stated.  
13—Entero-enterostomy later for perforated jejunal ulcer; died.

For otherwise healthy infants and children with chronic hemorrhage, perforation, pyloric occlusion or uncontrollable symptoms, operation is indicated, but children, like adults, are subject to the dangers of postoperative gastrojejunal ulcer.

Recovery is reported subsequent to the closure, 34½ hours after birth, of a perforated duodenal ulcer in a colored, male infant. The child is well, six years afterward.

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## SURGICAL PROBLEMS IN THE TREATMENT OF GASTROJEJUNAL ULCERATION\*

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It will probably be conceded that the operation of gastro-enterostomy still occupies an important rôle in the surgical treatment of duodenal ulcer. In the majority of instances, the patients are definitely relieved of their symptomatology, because the duodenal lesion is usually healed by this simple procedure. In any series of cases, however, there are some unsatisfactory results, patients in whom the postoperative train of symptoms is often materially worse than those which originally brought them to operation. Most of these serious complaints may be attributed to the effects of gastrojejunal ulceration. The appearance of this complication following gastro-enterostomy has long been recognized, but it is only recently that the frequency of marginal and jejunal ulceration has been fully appreciated. However, the occurrence of gastrojejunal ulceration is not solely confined to gastro-enterostomy. It may occasionally follow a gastrectomy of the Billroth II-type for duodenal ulcer.

It was thought that it might be of interest to discuss the subject of gastrojejunal ulceration as it occurs in the ward patients of a general hospital, placing special stress on the surgical problems which may complicate its treatment.

The therapeutic approach to this problem demands an intimate knowledge of the pathology and pathologic physiology induced by these lesions. It is important to know the extent, character, and location of the ulceration. There may be one or more ulcers present. These may be located in the margins of the stoma, usually on the jejunal side and rarely the gastric. Ulceration may occur opposite the stoma, or a short distance from it, most often in the efferent rather than the afferent jejunal loop. The ulcer may be either superficial, simulating an erosion, or deep, with a definite crater. In either variety, if the blood vessels are involved, hemorrhage may be a serious complication. While the jejunal and marginal ulcers may perforate either into the free peritoneal cavity or into the colon, causing a gastrojejunocolic fistula, it is more usual for these penetrating ulcers to be effectively walled-off by the adherence either of the transverse mesocolon, the colon, intestines, or pancreas. This may result in a large intra-abdominal inflammatory exudate.

Occasionally, the inflammatory reaction about an area of ulceration may be so severe and extensive that either an acute or subacute obstruction of the gastro-enteric stoma or the efferent loop may result. In some cases, even

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though this acute inflammation eventually subsides, the resulting scar tissue may produce some degree of obstruction. Obstruction in the stomal region, especially if accompanied by either a pyloric spasm or a duodenal stenosis usually produces a dilatation of the stomach. The gastric wall under these circumstances may eventually become atonic. The resulting inability to retain food, and the loss of gastric secretions by vomiting lead to nutritional disturbances such as an avitaminosis and an hypoproteinemia and to dehydration and an alkalosis which may become so severe as to threaten life.

The symptomatology of this disease as a rule is rather typical, and the diagnosis of gastrojejunal ulcer rarely occasions great difficulty. There is the usual antecedent ulcer history for which a gastro-enterostomy or a partial gastrectomy was performed, a few weeks or many years before the onset of the present trouble. This is described as a recurrence of the epigastric pain often so severe in its radiation to the back that morphine is required for its alleviation. Food usually aggravates the condition, with the result that appetite becomes less and weight is lost. Occasionally, the element of pain, especially in the hyposensitive individual, is overshadowed by the sudden occurrence of either a profuse hematemesis or a marked melena. While these hemorrhages may be alarming, they rarely lead to a fatal issue. Acid eructations, persistent nausea, and occasional vomiting, especially after the ingestion of food are frequent symptoms. Vomiting, however, may be a presenting and persistent symptom in the presence of stomal obstruction and gastric ileus.

The sudden occurrence of fecal vomiting, foul eructations, and persistent diarrhea, with or without antecedent pain, usually heralds the perforation of a jejunal ulcer into the transverse colon. This is a very serious complication for, unless the gastrojejunal fistula is corrected surgically, death from inanition will result quite rapidly.

Occasionally, the onset of terrific abdominal pain associated with nausea, vomiting, and the physical findings of shock, board-like rigidity, and generalized tenderness of the abdomen make a diagnosis of a perforated jejunal ulcer most likely. While a plain roentgenogram of the abdomen will not always disclose the presence of free air under the diaphragm, an abdominal puncture will invariably yield the presence of bile-tinged fluid.

Roentgenographic studies following the ingestion of a barium meal are invaluable in confirming the clinical diagnosis. These may be of inestimable aid in planning a therapeutic course. Their interpretation, to be sure, often requires unusual skill. Tenderness in the region of an irregular stoma while the patient is being fluoroscoped, a dilated stomach with retention of barium, suggestive of hypomotility or obstruction, the presence of barium patches in the jejunum, indicative of ulcer pockets, a stenosis or irregularity of either the afferent or efferent loops are helpful in the establishment of a diagnosis. The passage of a barium meal directly from the stomach outlining the colon concretely establishes the presence of a gastrojejunal fistula.

Gastroscopic examination with the flexible Schindler instrument has proved of considerable value in many of the more obscure cases. Areas of

either actual gastrojejunal ulceration or the presence of scarring about the stoma may be distinctly seen. In addition to this, the presence of either an acute or chronic gastritis may aid in differentiating the clinical picture.

Fractional test meals are of confirmatory value because in the majority of these patients who have a constitutional tendency to develop ulcers the total acidity and free hydrochloric acid are usually high. Gastrojejunal ulceration in the presence of an anacidity is almost unknown. A study of the blood plasma chlorides and the  $\text{CO}_2$  combining power are important, for occasionally a severe alkalosis may be present without clinical manifestations.

The physical examination rarely discloses anything definite except deep supra-umbilical tenderness slightly to the left of the median line.

Once a diagnosis has been made of a gastrojejunal ulcer following either a gastro-enterostomy or a partial gastrectomy, any of the accepted medical methods of ulcer therapy should be tried first. These patients cannot be treated satisfactorily by ambulatory methods. Hospitalization with absolute bed rest must be insisted upon, if there is any possibility of effecting a "medical cure." If hemorrhage is present as a complicating factor, treatment either by absolute gastric rest and blood transfusions or by the diet advocated by Muelengracht may be tried. In cases of a gastric or a high jejunal obstruction with alkalosis, daily lavages of the stomach and the parenteral administration of adequate amounts of saline, glucose, and blood are essential. In cases of gastric atony, the return of gastric tone can best be estimated by a diminution in the amount of gastric retention, the elevation of the blood chlorides to normal, and a reduction in the  $\text{CO}_2$  combining power of the plasma.

Many of these patients are undoubtedly healed by medical treatment, if not permanently at least temporarily, and many are improved following a course of treatment, thereby becoming better risks for operation. However, if medical treatment after a fair trial does not give satisfactory relief, or if the economic situation of the patient is such that the pattern of life cannot be made to conform with the dietary demands involved and with the routine of treatment prescribed, or if acute obstructive complications incident to jejunal ulceration are present, surgery is indicated.

Naturally, if an acute jejunal ulcer perforates into the free peritoneal cavity, immediate surgery is required, and if the perforation occurs into the transverse colon, intervention is indicated as soon as the physical condition of the patient will permit.

The surgical management of gastrojejunal ulceration and its complications depends mainly upon the pathology present at the time of operation, the surgical procedure naturally being adapted to the physical condition of the patient. With this as a basis, it may be convenient to divide arbitrarily these cases into certain groups:

- (1) Acute perforated gastrojejunal ulcers.
- (2) Resectable gastrojejunal ulcers following gastro-enterostomy.
- (3) Massive gastrojejunal ulcers following gastro-enterostomy.

- (4) Cicatrized gastrojejunal ulcers following gastro-enterostomy.
- (5) Resectable gastrojejunal ulcers following partial gastrectomy.
- (6) Gastrojejunal ulcers following radical subtotal gastrectomy.
- (7) Gastrojejunocolic fistulae.

(1) *Acute Perforated Gastrojejunal Ulcers*.—The symptomatology and physical findings of this condition are similar to that seen in perforated gastroduodenal ulcers. Once this diagnosis has been established, surgical exploration is indicated immediately. A small ulcer in the efferent jejunal loop, close to the gastro-enterostomy stoma, which has perforated into the free peritoneal cavity is usually found without difficulty. A simple closure of the perforation was all that was attempted, more radical surgery being left for the future (Case 1).

**Case 1.**—History No. 429566: B. W., age 54. Admitted May 20, 1940. Died May 30, 1940.

1935—Posterior gastro-enterostomy for duodenal ulcer.

1938—Suture of a perforated gastrojejunal ulcer.

1940—Subtotal gastrectomy, with antecolic Hofmeister terminolateral gastrojejunostomy and jejunorrhaphy for jejunal ulcer, and Witzel jejunostomy.

In 1935 a posterior retrocolic gastro-enterostomy had been performed because of a duodenal ulcer. He was completely relieved of symptoms following this operative procedure until two weeks before admission, when he had a recurrence of epigastric pain coming on three or four hours after meals. On the morning of admission, September 13, 1938, he was suddenly seized with severe generalized abdominal pain which steadily increased in severity. There was nausea but no vomiting. A right inguinal hernia and absent testicle had been known for many years. Following the attack of pain, the inguinal mass became larger than usual, painful, and could not be reduced. He was admitted to the service of Dr. A. Hyman.

Physical examination revealed an acutely ill, prostrated male. The teeth were carious. The lungs showed diffuse musical râles, heart slightly enlarged. Blood pressure 130/90. Abdomen was generally spastic, more so in the lower quadrants, right greater than left. There was also generalized abdominal tenderness, and rebound. There was a tender mass in the right inguinal canal which could not be completely reduced. Right testicle was absent from the scrotal sac. No obliteration of liver dullness. White count 23,900, with 81 per cent polys. Hemoglobin 92 per cent. Urine negative.

The differential diagnosis lay between torsion of an intra-abdominal testicle or perforated gastrojejunal ulcer. Celiotomy was immediately performed through a right lower quadrant midrectus incision, which exposed the external ring. An hemorrhagic, inflamed hernial sac was visualized. The sac was mobilized and opened, revealing large quantity of greenish fluid. A small testicle was seen and resected, herniorrhaphy performed, and then the upper abdomen was explored, which disclosed a perforation of a gastrojejunal ulcer. Repair was effected. Patient's postoperative course was remarkably good, and he was discharged on the fourteenth postoperative day, April 27, 1938.

He continued to complain of abdominal pain after meals and was readmitted, May 20, 1940, at which time Rehfuess test meal showed a free acid of 80 and total of 90 units. Roentgenograms revealed the presence of a jejunal ulcer and a 40 per cent gastric residue after three hours. He was reexplored, under spinal anesthesia. The stomach was dilated to two and one-half times its normal size. On the anterior wall of the jejunal side of the stoma, a penetrating jejunal ulcer, sealed-off by a thickened transverse mesocolon, was found. A subtotal gastrectomy, with an antecolic Hofmeister terminolateral gastrojejunostomy, and an excision of a jejunal ulcer, with a jejunorrhaphy was performed.

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Because of the atonic stomach, a Witzel jejunostomy was done. He developed a bronchopneumonia of both lower lobes. Sulfapyridine was given in full doses through the jejunostomy, as well as Type III antipneumococcus serum. He died three days after operation. P. M. No. 70865: Confluent bronchopneumonia.

(2) *Resectable Gastrojejunal Ulcers Following Gastro-enterostomy.*—An adequate preoperative preparation of these patients, as well as all groups suffering from this disease, is most essential. Careful attention was paid to the oral hygiene. The diet was adequate in its protein and vitamin content. Sufficient fluids were given by mouth, supplemented if necessary by the parenteral administration of saline, glucose, and blood. If gastric retention was not present, the stomach was lavaged only once, *i.e.*, six hours before operation.

There appears to be no ideal anesthesia because, regardless of the method, the incidence of pulmonary complications is unfortunately extremely high, and often the cause of death. Our best results seemed to have been obtained with spinal anesthesia with Jones' solution, combined with pentothal intravenously. In cases which were unusually poor risks, a field block of the upper abdominal wall with novocain was supplemented by either cyclopropane or ethylene anesthesia.

Past experiences with the surgery of gastrojejunal ulcers have taught us that if better and more satisfactory follow-up results are to be expected, certain operative procedures must be discarded. Excision of the marginal and jejunal ulcers with some type of plastic repair, another gastro-enterostomy in addition to the existing one, and separation of the old gastro-enterostomy with the formation of a new one, are of little permanent value in the presence of active ulceration. Under certain circumstances, these palliative procedures may prove useful until the condition of the patient improves sufficiently to tolerate more radical surgery. Simple separation of the gastro-enterostomy stoma and the excision of the jejunal ulcer as a definitive procedure in the treatment of gastrojejunal ulceration is ultimately unsatisfactory in most instances. It is invariably followed by a reactivation of the duodenal ulcer, or possibly a gastric ulcer, with a recurrence of all the previous symptoms (Case 2).

**Case 2.**—History No. 453891: A. B., age 38. Admitted March 18, 1940. Discharged March 31, 1940.

1920—Gastro-enterostomy for duodenal ulcer.

1940—Disconnection of gastro-enterostomy, gastrorrhaphy, and jejunorrhaphy for jejunal ulcer.

1940—Subtotal gastrectomy with Hofmeister terminolateral gastrojejunostomy (antecolic) for duodenal ulcer.

This is the fourth admission of a male who had had a gastro-enterostomy performed in 1920 for a duodenal ulcer. He remained well until 1934, when he developed upper abdominal pain, and the following year roentgenography revealed a marginal ulcer. He was relieved by medical therapy until 1939, when the pain recurred, this time accompanied by bleeding. Since then, he has had epigastric pain intermittently. A gastro-intestinal series taken in August, 1939, and in January, 1940, revealed an incomplete



obstruction and an ulcer in the distal jejunal loop, about two inches from the stoma. There was a small three-hour retention.

Physical examination revealed an obese but well-developed male. Blood pressure 126/60. There was tenderness in the right upper quadrant and epigastrium, and scars of previous operations for bilateral inguinal herniae, and of the previous gastro-enterostomy. Hemoglobin 96 per cent. There was a gastric retention of 100 cc. The Rehfuß test meal showed a 44 free acid, and total of 52 units. The fasting contents contained a free acidity of 10, and total of 40 units. Blood urea 12 mg.; blood sugar 116 mg.; plasma chlorides 620 mg., carbon dioxide 48 vol. per cent. The blood Wassermann was negative. The urine was negative.

Exploration was performed, under avertin and ethylene anesthesia, March 21, 1940, through a median epigastric incision. The stomach and duodenum were found adherent to the previous right epigastric incision. The gastro-enterostomy stoma was markedly narrowed, evidently from previous ulceration. There was definite constriction of the efferent loops with marked dilatation of the afferent. The region of the duodenum was friable and showed signs of old healed ulceration. The gastro-enterostomy was disconnected. A gastrorrhaphy was performed. The jejunal ulcer was excised and a transverse jejuno-rhaphy was done. Because the condition of the patient was not entirely satisfactory at this stage, no further surgery was attempted.

The postoperative course was satisfactory. He was discharged on the tenth day after operation.

Patient was well for about two months after his operation, and then developed a recrudescence of the symptoms resembling his previous duodenal ulcer. A Rehfuß test meal showed a free hydrochloric acid of 40, and a total of 70 units.

He was readmitted in June, 1940, at which time a subtotal gastrectomy of the Hofmeister type, with a terminolateral gastrojejunostomy was performed for chronic gastric ulcer. Following this he made an uneventful recovery.

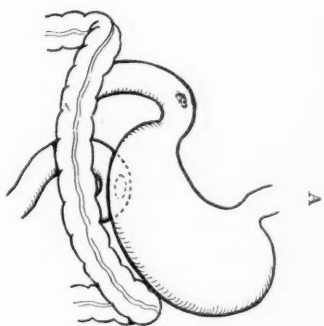
When last seen, January 8, 1941, he had no further complaints.

Therefore, in the surgical treatment of gastrojejunal ulcer an attempt should be made to insure the patient, if at all possible, against subsequent ulceration in the stomach, duodenum, or jejunum. Ulceration in these areas is not apt to occur in the presence of an anacidity. Anacidity, or low acid values, are most frequently obtained by an excision of the acid stimulating pylorus and antrum, and as much of the acid secreting fundic portion of the stomach as possible. The resection of the diseased area involved in the gastrojejunal ulceration, supplemented by a radical subtotal gastrectomy of the Billroth II-type theoretically, and at present, best fulfills this requirement.

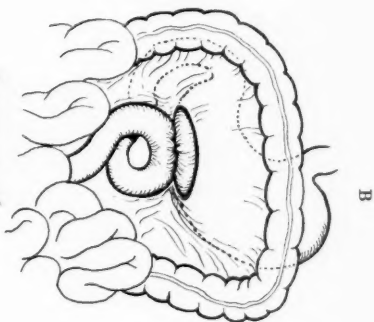
The performance of a primary subtotal gastrectomy is not an easy technical procedure at best, but in the presence of a gastrojejunal ulceration, it is fraught with innumerable additional dangers—hazards which can only be partially eliminated with increased experience and particular attention to surgical minutiae. The operation should be so planned that it may be successfully terminated at certain stages should the physical condition of the patient not warrant its completion (Case 2). For this reason we have divided the operation into two main parts: I. The separation of the gastro-enterostomy. II. Subtotal gastrectomy.

1. Separation of the gastro-enteric anastomosis, followed by:
  - (a) Gastrorrhaphy.

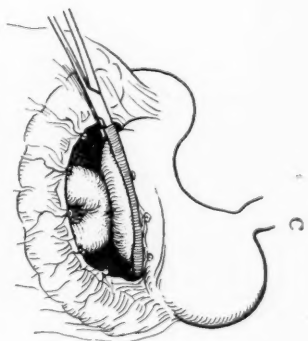
# GASTROJEJUNAL ULCERATION



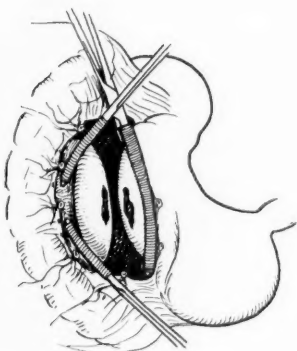
Posterior gastroenterostomy  
for duodenal ulcer



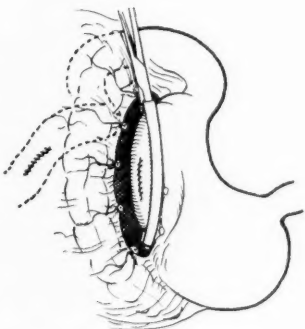
Exposure of  
gastroenterostomy



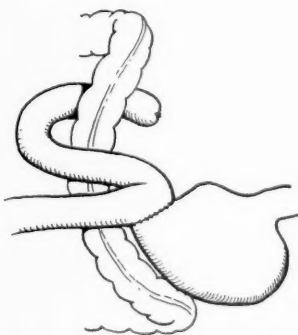
Exposure of liberated stoma  
through the lesser omental sac



Separation of stoma



Gastrorrhaphy and  
jejuno-rhaphy



Hoffmeister subtotal gastrectomy  
with antecolic termino-lateral  
gastrojejunostomy

PLATE I.—Drawings illustrating the operative procedures employed in the separation of the gastro-enteric stoma.

(b) Excision of the jejunal ulcer with restoration of jejunal continuity by:

- (1) Jejunorrhaphy.
- (2) End-to-end jejunojejunostomy.
- (3) End-to-side jejunojejunostomy.
- (4) Side-to-side jejunojejunostomy.

2. Subtotal gastrectomy of the Hofmeister-type with terminolateral gastrojejunostomy either anterior or posterior to the transverse colon.

I. *Separation of the Gastro-enteric Anastomosis.*—(a) In order to identify the retrocolic posterior gastro-enterostomy (which was the most common type of previous procedure) the greater omentum was completely freed from the adhesions which invariably bound it to the previous abdominal incision and other intra-abdominal viscera. Following this, it was possible to bring the transverse colon and its mesentery upward and forward, thereby exposing the jejunal portion of the stoma. Then, the field of operation was carefully walled-off and protected by hot, moist pads. The dense adhesions in this area were carefully divided by knife dissection, liberating the afferent and efferent jejunal loops. The anterior margin of the adherent transverse colon was dissected free, exposing the gastric side of the stoma (PLATE I B). Frequently while liberating the anterior part of the anastomosis, areas of acute ulceration were entered, with the escape of intestinal content. If perforation did occur, it was temporarily closed by sutures. At this point, we usually found it advisable to enter the lesser omental sac by horizontally dividing the gastrocolic omentum in the region of the stoma. The anastomosis was then more easily mobilized laterally, and posteriorly from its attachment to the transverse mesocolon, great care being taken to preserve the integrity of the middle colic vessels. If ulceration was present in this location, the resulting edema and induration often caused a thickening of the transverse mesocolon with marked distortion of the normal anatomy. Once the anastomosis was freed completely, it could be easily delivered through the lesser omental sac, provided the afferent jejunal loop was sufficiently long (PLATE I C). If this loop was short, the anastomosis was drawn downward below the transverse mesocolon so that it could be adequately controlled during its separation.

The stomach was then carefully separated from the jejunum, "spilling" being avoided either by the application of a curved rubber clamp to the bowel or the judicious use of suction (PLATE I D). The gastric opening was immediately closed with a Connell inversion suture of chromic catgut reinforced with a continuous Lembert-Pagenstecher suture (PLATE I E). This step, if a gastrectomy was to be subsequently performed, may appear unnecessary to some, but it is an added precaution in the maintenance of peritoneal asepsis.

(b) Excision of the jejunal ulcer and restoration of jejunal continuity: The disconnected loop of open jejunum was then carefully inspected. If the ulcer was small, the lesion was excised locally, and in many instances the entire mesenteric border of jejunum was left undisturbed. In cases such as these, a transverse jejunorrhaphy restored the lumen of the bowel (PLATE I

E). However, partial jejunectomy became necessary when the ulceration either involved the circumference of the bowel or penetrated into its mesentery. Extensive scarring with stenosis of the bowel occasionally called for an intestinal resection.

Jejunojejunostomy, similar to intestinal anastomosis, is beset with two great dangers: leakage and obstruction at the site of the anastomosis. Leakage may be prevented by the careful preservation of the blood supply to the bowel and the accurate surgical approximation of its walls. Obstruction may be partially eliminated by selecting that type of anastomosis which will insure an adequate lumen, thereby eliminating the possibilities of obstruction with the serious sequelae of back pressure on the duodenal and jejunal suture lines. An end-to-end anastomosis was the most frequently used procedure. Occasionally, in the presence of a retrocolic, no-loop, posterior gastrojejunostomy, certain technical details made this type of jejunal restoration impractical. The proximity of the anastomosis to the ligament of Treitz, and the duodenojejunal angle, increased the hazards of an end-to-end suture. Under these circumstances, we have implanted the open end of proximal jejunum into the side of the distal jejunum (Case 3). In other cases, when a marked disparity existed in the diameter of the afferent and efferent jejunum, a side-to-side anastomosis was performed (Case 6).

A certain amount of local edema is apt to follow any type of intestinal anastomosis. Some surgeons have advocated the introduction of either a Levin tube or its modification through the new gastrojejunostomy and *via* the jejunojejunostomy to the region of the duodenal stump, in order to reduce the accumulation of gas and fluid in this blind end. Theoretically, this may be a good suggestion, but, practically, we have found it difficult, and at times impossible, to thread effectively a Levin tube along this devious channel and maintain strict asepsis.

Occasionally, following the separation of the gastrojejunal anastomosis and closure of the gastric defect and the restoration of jejunal continuity, the physical condition of the patient did not safely permit further surgery. The operation was then terminated successfully at this point, after the closure of the rent in the transverse mesocolon and the gastrocolic omentum (Case 2). However, in the average case, it was usually possible to proceed with the subtotal gastrectomy.

II. *Subtotal Gastrectomy.*—This part of the operation rarely presented unusual difficulty. The technic which was followed was essentially that which has been previously described by Dr. A. A. Berg.<sup>1</sup> The stomach was usually transected at a point well proximal to the reentrant angle, and high on the greater curvature. The resection must be radical, subtotal in its extent; any lesser resection, we feel, is to be condemned. While it is undoubtedly important to measure the gastric segment which has been resected, it is more important to leave as little of the stomach as is consistent with safety. Inasmuch as the previous gastro-enterostomy has usually healed the duodenal ulcer, the excision of the ulcer-bearing area, and closure of the distal duodenum were

usually quite simple. The duodenal stump was regularly drained with rubber dam, which was brought out through a right subcostal stab wound. There were no cases in which any postoperative complications could be ascribed to the drainage. However, there were a few in which a small duodenal leak was effectively drained externally, thereby preventing the hazards of a generalized peritonitis.

Gastro-intestinal continuity was restored by the Hofmeister modification of the Billroth II-type of procedure, with a terminolateral gastrojejunostomy. Whether this anastomosis was made either anterior or posterior to the colon seemed to be of little importance. No difficulties have been noted either in the immediate postoperative course or in the follow-up observations of either type of anastomosis. We are at present employing the anterior type more, because if further gastrojejunal ulceration should develop, the technical difficulties of any subsequent surgery are definitely lessened (PLATE I F).

The abdominal incision, usually a median epigastric one, was closed with interrupted, through-and-through heavy silk sutures. This type of closure has been employed for many years, and has proved to be an excellent prophylactic measure against wound dehiscence and evisceration.

Following the return to the wards, the Levin tube, which was introduced intranasally into the stomach at the time of operation, was aspirated every two hours. Parenteral fluids, which were administered throughout the operation, were continued, supplemented by blood transfusions if necessary. Fluids were allowed by mouth after 24 hours. Intravenous saline and the Levin tube were discontinued when sufficient quantities of fluid were taken by mouth, and were retained.

### (3) *Massive Gastrojejunal Ulcers Following Gastro-enterostomy.*—

There were certain types of gastrojejunal ulcers in which persistent vomiting, resulting in alkalosis, was a prominent symptom. After the adequate pre-operative preparation already referred to, exploration was performed. Often an active penetrating ulceration was found which caused an extensive productive inflammatory reaction in the neighborhood of the anastomosis, resulting, occasionally, in either an acute or subacute obstruction in the region of the stoma. Any radical surgery entailing extensive dissection in this acutely infected, friable, and edematous tissue would probably have caused a rapid spread of a fatal peritonitis. In conditions such as this, we have been ultra-conservative. A Witzel jejunostomy was performed for alimentation and as a palliative procedure (Case 3). Jejunal feedings of proper content and sufficient caloric requirement usually caused a definite physical improvement in these patients. Gastric digestion was practically eliminated, giving the stomach a certain amount of physiologic rest. In the interim, a period of four to 12 weeks, the marked inflammatory reaction which was previously present about the area of ulceration either subsided, or the ulcers were healed completely, so that at the time of reexploration, a previously inoperable condition became operable. A subtotal gastrectomy could be performed now without undue risk. Many surgeons have condemned jejunostomy



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because it may result in leakage with a fatal peritonitis, and occasionally in acute intestinal obstruction. If a jejunostomy is properly performed there should be no danger from either of these two complications. It is important, however, that the jejunostomy be performed at least 18 to 22 inches from the duodenal angle and that the enterostomy tube be brought out through a left subcostal stab wound. These precautions eliminated any interference with a subsequent subtotal gastrectomy. Following this operation the jejunostomy tube may be removed as soon as gastric alimentation is restored.

**Case 3.**—History No. 432385: L. K., age 55. Admitted November 29, 1938. Discharged April 2, 1939.

1915—Suture of a perforated gastric ulcer, with posterior retrocolic gastro-enterostomy. (January)

1915—Excision of a duodenal ulcer, with pulse-string occlusion of the pylorus. (August)

1916—Exploratory celiotomy for high intestinal obstruction, due to multiple adhesions.

1938—Jejunostomy for alimentation, because of pyloric stenosis, with occlusion of the gastro-enterostomy stoma by massive jejunal ulceration. (December)



CASE 3.—Roentgenogram demonstrating massive jejunal ulceration with penetration.

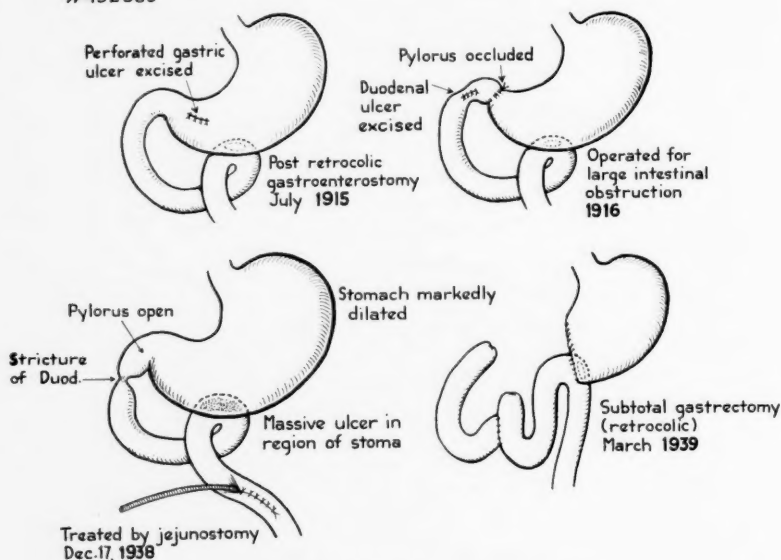
1939—Subtotal gastrectomy, with posterior retrocolic terminolateral gastro-enterostomy of the Hofmeister type, and partial jejunectomy, with end-to-side jejunojejunostomy for healed gastrojejunal ulcer. (March)

This is the first admission of a male, age 55, who for the past 24 years has had ulcer symptoms. In 1914, an appendicectomy was performed for chronic appendicitis. In January, 1915, he perforated a gastric ulcer and at that time, in addition to a suture of the ulcer, a posterior retrocolic gastro-enterostomy was performed. In August, 1915,

he was reexplored because of persistent ulcer symptoms and at that time a small ulcer on the anterior wall was excised and a purse-string occlusion of the pylorus was performed. In 1916, he was again operated upon because of high intestinal obstruction, due to multiple adhesions. He was then well until about three months before admission, when he began to have recurrence of his ulcer pain, and two weeks before admission there was persistent nausea, vomiting, and severe abdominal cramps.

Physical examination disclosed a man, cadaverous in appearance, in marked distress, complaining of severe cramp-like abdominal pain. Teeth were in poor condition and there was marked pyorrhea. Abdomen was soft. There was acute epigastric tenderness.

#432385



CASE 3.—Schematic view of operative procedures.

The scars in his left upper quadrant and upper midabdomen, and lower right quadrant were well healed. Hemoglobin 75 per cent. Blood pressure 105/70. Blood urea 25 mg.; blood chlorides 505 mg.;  $\text{CO}_2$  71 vol. per cent. Total blood proteins 5.6. Blood Wassermann was negative. Urine examinations were negative, and the stools were four plus guaiac. A Rehfuess test meal showed free acid of 55 units and total acidity of 75, and blood was present. A gastro-intestinal series showed marked pyloric stenosis and a very narrow and deformed gastro-enterostomy stoma, with a definite pocket in the jejunum just distal to the stoma. There was marked residue after six hours. Gastroscopy revealed that the gastro-enteric stoma was patent, and there was a marked atrophic and marked localized hypertrophic gastritis. Lavage of his stomach on several occasions revealed retention of 1,000 to 3,000 cc. Because of the persistence of his vomiting, the marked retention, the intractable pain, and the fact that he was losing ground, surgical exploration was performed, December 7, 1938, under local anesthesia and ethylene. The stomach and transverse colon were dissected from the anterior abdominal wall and from the under-surface of the liver. A lesion about the size of a large walnut was found in the region of the gastro-enterostomy stoma, evidently due to a posterior jejunal ulcer. Because of the marked inflammatory reaction which was present and poor surgical condition of the patient, a Witzel type of jejunostomy for jejunal alimentation was performed about 18 inches from the gastro-enteric stoma, and the tube was brought out through a left subcostal stab incision.

The patient did not do well immediately after operation because of severe infection

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of the anterior abdominal wall, and in addition to his jejunal feedings of Scott-Ivy pabulum he was given supportive treatment of blood transfusions and glucose intravenously. Following rest and gastric lavage, the retention gradually diminished. Gastroscopy at this time showed a slight improvement, inasmuch as there was less inflammatory reaction about the stoma. A gastro-intestinal series at this time showed that the jejunal ulcer which had been previously noted was definitely smaller and, although there was still more than 50 per cent residue at the end of six hours, much barium was seen to pass through the pylorus.

His general condition improved sufficiently so that about three months after the preliminary jejunostomy he was reexplored, March 8, 1939. The stomach was again found adherent to the anterior abdominal wall, as well as the omentum. The duodenum was adherent to the under surface of the liver. The stomach was dilated to two and one-half times normal size, and its walls were markedly atrophic. About one-half inch distal to the pylorus, there was a marked stenosis of the duodenum, evidently the site of the previously excised ulcer. In the region of the gastro-enterostomy stoma, the afferent loop was especially short and dilated, and at a point slightly distal to the stoma there was a definite stenosis, almost leading to a complete occlusion of the efferent loop. About six inches farther along, there was a kinking of the jejunum. The marked inflammatory reaction which had been noted at the previous exploration had completely disappeared. There was no evidence of an active jejunal ulcer. All that remained was a scar almost occluding the efferent jejunal loop. A subtotal gastrectomy, with Hofmeister terminolateral retrocolic gastrojejunostomy was performed for a healed duodenal ulcer, and a partial jejunectomy, with an end-to-side jejunojejunostomy, was performed for a healed jejunal ulcer of the efferent loop.

The postoperative course was fairly smooth, the only complication being a mild wound infection. Jejunostomy was maintained for feeding purposes until the patient could take adequate diet by mouth, and the enterostomy tube was removed 11 days after operation. He has been unusually well, and has gained almost 40 pounds. He has had no symptoms referable to his gastro-intestinal tract when last seen, April 10, 1940.

(4) *Treatment of Cicatrized Stomal and Jejunal Ulcers Following Gastro-enterostomy.*—This group usually was in urgent need of surgery. These were the patients who were not suffering solely from the effects of acute ulceration, but rather from the effects of gastric obstruction incidental to the cicatricial contraction of marginal and efferent jejunal ulcers. These patients, as a rule, were so dehydrated and debilitated by long periods of intermittent vomiting that even if the chemical imbalances were adequately corrected, the shock of any extensive surgery would have terminated disastrously. In this group, either some simple corrective measure aimed to relieve the obstruction, or a jejunostomy for alimentation was performed in order to temporarily relieve the patient until an improved physical condition would permit more radical surgery, should it be deemed necessary. If, at the time of exploration, the pylorus was patent and the extensive scarring of previous jejunal ulceration had produced a stenosis of either the stoma or the efferent jejunal loop, a properly placed entero-enterostomy appeared to be all that was necessary to relieve the symptoms. The physical condition of the patient improved following this simple procedure. If active jejunal ulceration should recur subsequently, radical surgery could be undertaken then under more auspicious circumstances (Case 4).

**Case 4.**—History No. 439460: W. E., age 60. Admitted May 12, 1939. Discharged June 25, 1939.

1919—Posterior retrocolic gastro-enterostomy for bleeding duodenal ulcer.

1923—Appendicectomy for chronic appendicitis.

1939—Jejunojejunostomy for obstruction of distal jejunal loops, due to jejunal ulcer.



CASE 4.—Roentgenogram showing obstruction of efferent jejunum, with marked dilatation of stomach, duodenum and afferent jejunum.

This is the first admission of a patient who, since age 16, has had multiple episodes of epigastric pain which were usually followed by hematemesis and black stools. These occurred at intervals of six to eight months. Twenty years ago, he had had a posterior gastro-enterostomy for duodenal ulcer. Four years later, after a severe hemorrhage, he had another celiotomy, at which time a diseased appendix was supposed to have been removed. Three years before this admission he was treated at another hospital for massive hemorrhages. Four months before the present admission he began to complain of severe epigastric pain radiating to the right upper quadrant, nausea, and vomiting. The vomitus consisted of the food ingested from previous meals. Five weeks before admission he had a severe hemorrhage.

Physical examination disclosed a rather pale and chronically ill male. There was moderate peripheral sclerosis. Blood pressure 140/80. There was tenderness and pressure in the epigastrium and a well-healed upper right rectus scar extending from the ensiform to below the umbilicus. Hemoglobin 67 per cent. R.B.C. 3,000,000 W.B.C. 3,000,

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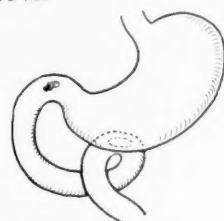
with normal differential. Sedimentation time one hour, four minutes. Urine: Specific gravity 1036, faint trace of albumin, occasional hyaline casts. Blood urea 11 mg., blood sugar 100 mg.; blood chlorides 620 mg.; the  $\text{CO}_2$  combining power 75 vol. per cent. Icteric index 6; total blood proteins 5.7 mg. The Rehfuess test meal free acid 35 units, total acidity of 48. Electrocardiogram showed slight depression of the RT. transition in leads II and III.

A gastro-intestinal series showed a gastro-enterostomy. The barium which was ingested almost all passed to the proximal loop, causing the duodenum to become markedly dilated. The duodenal bulb was markedly deformed. The first one and one-half inches of distal jejunum was markedly narrowed, and showed the presence of a small ulcer pocket. At the end of six hours there was a 20 per cent residue.

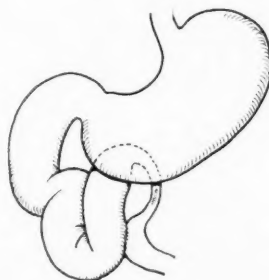
The gastric retention was treated conservatively with lavage, and intravenous fluids were administered liberally. Retention was markedly diminished, and after two transfusions, hemoglobin was elevated to 80 per cent.

On May 7, 1939, an exploratory celiotomy was performed, under local field-block and ethylene. There were innumerable adhesions from the omentum to the anterior abdominal wall. The stomach in the region of the pylorus and duodenum was adherent to the under surface of the liver by fine, dense adhesions, which were freed. There was

#439460



Posterior  
gastroenterostomy  
for duodenal ulcer  
1918



Jejunojejunostomy  
for stenotic ulcer of  
distal jejunal loop  
1939

CASE 4.—Schematic review of operative procedures.

no evidence of any active duodenal ulcer. On turning the transverse colon upward, adhesions were found completely occluding the afferent and efferent loops leading to the gastro-enterostomy. Upon freeing these, the stoma was exposed. On the anterior wall of the jejunum, occupying mainly the efferent loop, was a definite, acutely inflamed, jejunal ulcer which almost completely occluded the lumen, causing dilatation of the afferent loop to about four times normal size. Beyond the area of ulceration, the efferent loop appeared normal. A side-to-side jejunojejunostomy was performed between the dilated afferent and the small efferent loop, and about ten inches from this anastomosis a typical Witzel jejunostomy was performed for jejunal alimentation.

Following operation, gastric retention and alkalosis receded within three weeks. He had slight pitting edema of the ankles, at which time blood chlorides were about 610 mg. Parenteral saline was stopped at this point, and the edema disappeared, and blood chlorides fell to about 540 mg.

One month after operation, a gastro-intestinal series showed much less distention of the proximal loop of the jejunum and duodenum. The first one and one-half inches of the distal loop was constricted but no ulcer pocket was visible. There was no gastric retention. He was discharged asymptomatic on a Muelengracht diet, without any pain.

He was subsequently readmitted, August 8, 1939, and discharged on September 10, 1939, because of tarry stools. Following the operation he did well and gained 35 pounds.



During the two months he was at home, he followed a strict diet and gained in weight. He experienced an episode of dizziness, hematemesis, and melena on admission. He was well-developed and well-nourished; rather pale. Blood pressure 120/80, pulse 96. Hemoglobin 62 per cent, R.B.C. 4,400,000. W.B.C. 14,000, with a normal differential. Stools were guaiac positive. Urea 46. Urine was negative. Total protein 6.1. Hemoglobin dropped to 52 per cent, then to 42 per cent in the next few days, and he continued to have positive stools. Stools became guaiac negative on the thirteenth day, and the hemoglobin began to rise following four transfusions. He was placed on a Muelengracht diet while he was in the hospital. Surgery was not advised at this time.

When last seen, January 22, 1941, he had gained 46 pounds since operation, and looked amazingly well. He had no complaints.

There were instances in which the gastro-enteric anastomosis had become almost completely obliterated by extensive scarring, and, as a result, a new ulcer appeared with reflex pylorospasm. In this type of case, in which the condition of the patient was poor, the jejunum was easily separated from the stomach and its continuity was rapidly repaired, and a new gastro-enterostomy was performed. This appeared to be effective (Case 5). If, in addition either to the gastrojejunal obstruction, a pyloric spasm or a duodenal stenosis was present, the problem of a marked gastric dilatation complicated the picture. An adynamic gastric ileus as a postoperative complication is most serious. The constant retrograde drainage of duodenal contents into a dilated gastric pouch, often for weeks, is bound to result in marked intestinal disturbances and alkalosis. Under these circumstances, the operation of gastro-enterostomy was supplemented by a Witzel jejunostomy for alimentation. Many surgeons, in preference to jejunostomy, introduce a two-way tube at the time of gastro-enterostomy through the stoma into the efferent jejunum so that one part drains the stomach while the other part may be used for alimentation. Under ordinary circumstances, this tube is of undoubted value, but in conditions such as these described it possesses certain disadvantages. The tube, which often must be maintained in place for many weeks, may either become displaced or inadvertently removed quite early in the postoperative course. Occasionally, a decubitus ulcer of the larynx may result from its prolonged pressure. This complication is most unfortunate because it may result in either an edema of the glottis or a necrosis of the arytenoid cartilages. To avoid these various hazards and to assure alimentation during this critical period, we prefer a jejunostomy.

**Case 5.**—History No. 414414: A. I., age 57. Admitted October 1, 1937. Discharged November 2, 1937.

1931—Anterior gastro-enterostomy for duodenal ulcer.

1937—Disconnection of anterior gastro-enterostomy for healed jejunal ulcer, and posterior retrocolic gastro-enterostomy for gastric ulcer, with pylorospasm.

This patient has had abdominal pain since 1917. In 1931, he was operated upon for a duodenal ulcer. The extensive adhesions about the pylorus and duodenum prevented a radical operation, so that an anterior gastro-enterostomy was performed. He remained perfectly well until six months before admission, when he complained of epigastric pain and vomiting. He had a definite gastric retention at that time, which subsided following

## GASTROJEJUNAL ULCERATION

daily lavages. One month before the second admission, the pain recurred, and for the past week he vomited after every meal. He lost about eight pounds.

Physical examination revealed a very anemic and emaciated individual. There was a scar of a previous median incision. Peristaltic waves were present in the left upper quadrant, passing laterally toward the center of the abdomen. Hemoglobin 45 per cent. Blood urea 20 mg.; blood chlorides 500 mg.; carbon dioxide 62 vol. per cent. The gastro-intestinal series revealed a penetrating ulcer on the lesser curvature of the stomach, without marked pyloric obstruction. There was, however, an 80 per cent six-hour residue. There was no evidence of a patent gastro-enterostomy, but evidence of a jejunal ulcer. The Rehfuess test meal showed a free hydrochloric acid of 46 units.

Preoperatively, the patient was lavaged twice a day. He improved so markedly that his complaints almost subsided, and the residue dropped to zero.

On October 25, 1937, he was explored, under avertin and ethylene anesthesia. The stomach was fish-hook in appearance and was dilated to three times normal size. The stoma of the anterior gastro-enterostomy was contracted, and the site of a healed marginal ulcer. Below this, there was evidence of a previous entero-enterostomy. The previous gastro-enterostomy was separated without difficulty. The gastric opening was sutured. The jejunal orifice was used in the performance of a typical retrocolic gastro-



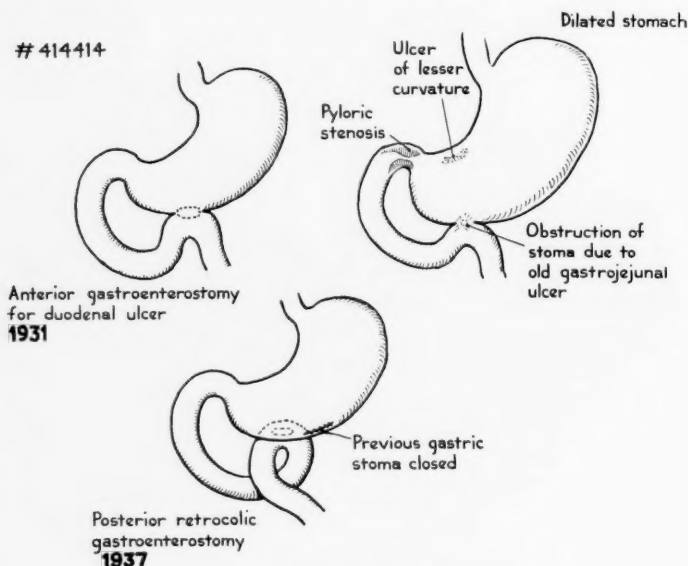
CASE 5.—Roentgenogram illustrating an almost complete obstruction of the gastro-enteric stoma.

enterostomy. The patient did perfectly well and, with the aid of three transfusions, had a normal convalescence. He was discharged on the thirteenth day.

Patient has been seen repeatedly, and when last seen, October 23, 1940, he weighed 159 pounds, and looked quite well. He had no specific complaints, and no vomiting.

(5) *Treatment of Resectable Gastrojejunal Ulcers Following Partial Gastrectomy.*—In the majority, the recurrent ulceration may be ascribed in part to the persistence of free hydrochloric acid, due most likely to an inade-

quate removal of the antrum, which was performed either purposefully or inadvertently. Some surgeons practice a minimum partial gastrectomy as a matter of choice; others in the course of a Schmilinsky procedure (Case 6).



CASE 5.—Schematic review of operative procedures.

**Case 6.**—History No. 453947: A. A., age 53. Admitted March 19, 1939. Discharged April 28, 1939.

1934—Retrocolic posterior gastro-enterostomy for duodenal ulcer.

1935—Schmilinsky operation for gastrojejunal ulcer.

1939—Secondary radical subtotal gastrectomy, with antecolic terminolateral gastroenterostomy and partial jejunectomy, with side-to-side jejunojejunostomy for multiple jejunal ulcers.

This is the first admission of a male, age 53, who was well until 13 years ago, when he developed preprandial pain, relieved by alkalis. Four years ago, a posterior retrocolic gastro-enterostomy was performed because of pain. He was improved after operation but noticed that, occasionally, the stools were tarry. One and one-half years ago he began to have episodes of epigastric pain accompanied by hematemesis. At this time, a diagnosis of gastrojejunal ulcer was made, and the Schmilinsky type of gastric and jejunal resection was performed. Following the operation, he bled profusely from the stomach, but this symptom gradually subsided until five months ago when severe epigastric pain recurred. During the month prior to admission he noted tarry stools.

Physical examination disclosed the fact that he was a well-developed, emaciated male, complaining of epigastric pain. There were two well-healed parallel scars in the right upper quadrant of the abdomen. Blood pressure 110/74; hemoglobin 75 per cent; blood chlorides 595 mg.,  $\text{CO}_2$  61. vol. per cent. Rehfuess test meal revealed a free acid of 90 units, total of 110. Stools were guaiac positive. A gastro-intestinal series showed a stomach upon which a partial resection had been performed. In the afferent jejunum, there was a constriction about one and one-half inches from the stoma, which was irregular. In the efferent loop, there was evidence of a penetrating jejunal ulcer. There was a delay in gastric emptying.

The patient was at first treated medically. In spite of almost constant milk drip,

## GASTROJEJUNAL ULCERATION

pain became so severe that operation was advised, and he was prepared with adequate doses of vitamins and desoxycorticosterone. On April 8, 1940, he was explored, under novocain field-block and cyclopropane anesthesia. There were omental adhesions to the anterior abdominal wall, and the resected stomach was bound to the under surface of the liver. It was normal in size. A healed jejunal ulcer was found at the jejunal site of the afferent loop as it entered the stomach and about one and one-half inches from this



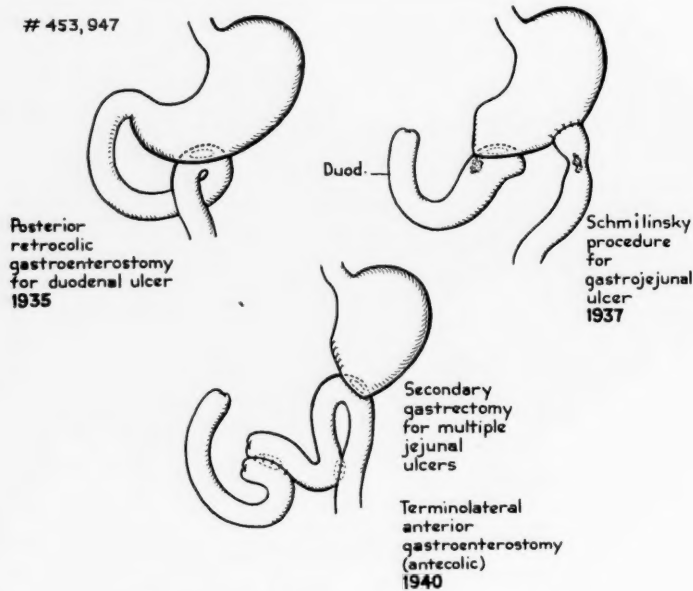
CASE 6.—Roentgenogram showing Schmilinsky procedure, with ulcer of afferent and efferent jejunal loops.

area was a slight constriction. A penetrating jejunal ulcer sealed-off by the transverse mesocolon was found in the efferent loop. Accordingly, both the jejunal loops were dissected free from the stomach. A partial resection of the jejunum which contained the ulcers was then performed, and the free openings were closed. Jejunal continuity was restored by a side-to-side jejunojejunostomy. A subtotal gastrectomy was then performed, removing 6 cm. of the lesser curvature and 11 cm. of the greater curvature, and an antecolic terminolateral gastrojejunostomy of the Hofmeister type was performed. Following the operation the patient did well, but his hemoglobin fell to 40 per cent, for which he received transfusions. The remainder of his course was complicated by a persistent gastric retention, which was treated by daily lavages and finally subsided. Wound healed and patient's symptoms were relieved. He was discharged on the seventeenth day.

When last seen, July 24, 1940, he had gained 50 pounds in weight. He was cautioned about the incessant use of tobacco.

In some of the recurrent cases in which a partial gastric resection followed a previous gastro-enterostomy, the surgeon left the previous gastro-enterostomy undisturbed, and simply removed that portion of the stomach which was distal to it. As a result a minimum resection was done (Case 7).

In all these cases in which a large gastric segment remains after a previous partial gastrectomy, the secondary gastrectomy must be more radical, provided that the gastrojejunal ulceration which is present is not so extensive



CASE 6.—Schematic review of operative procedures.

as to make the condition inoperable. If this condition existed, a preliminary jejunostomy was performed. The rationale of this procedure has been previously discussed.

**Case 7.**—History No. 423778: S. I., age 48. Admitted May 25, 1938. Discharged June 7, 1938.

1921—Excision of a duodenal ulcer, followed by gastro-enterostomy for pyloric obstruction.

1935—Partial gastrectomy, with preservation of old posterior retrocolic gastro-enterostomy for bleeding duodenal ulcer.

1938—Subtotal gastrectomy, with antecolic anterior Murphy button gastrojejunostomy, and entero-enterostomy for gastrojejunal ulcer.

This patient had had an excision of a duodenal ulcer in 1921, followed three weeks later by a pyloric obstruction, for which a posterior retrocolic gastro-enterostomy was performed. In 1935, following three episodes of melena, which were thought to be due to gastrojejunal ulcer, he was explored, and it was the operator's impression at that time that the cause of the hemorrhage was a bleeding duodenal ulcer. Accordingly, a partial gastrectomy was performed, leaving the old gastro-enterostomy intact. Since the last operation, he has had innumerable severe attacks of bleeding, all of which were treated symptomatically on previous hospital admissions. On the day before his present entrance to the hospital, he developed mild abdominal cramps followed by the passage of tarry stools and some bright red blood.

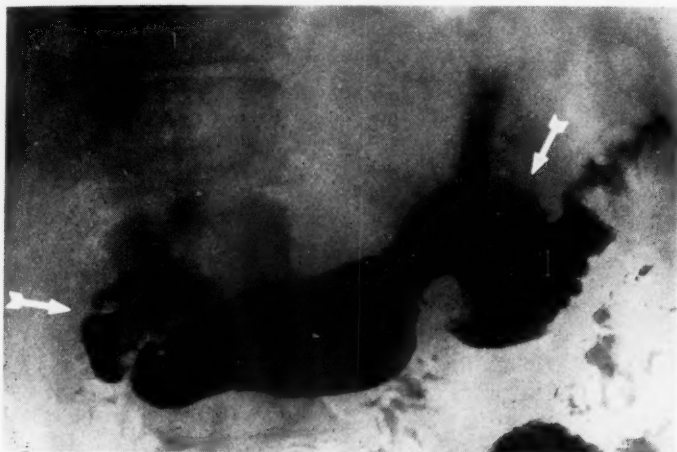
Physical examination revealed a pale individual, with some epigastric tenderness on deep pressure. Hemoglobin 75 per cent; W.B.C. 16,000, with 58 per cent polys; blood urea 20 mg., blood proteins 5.8 per cent. Following two transfusions, hemoglobin was



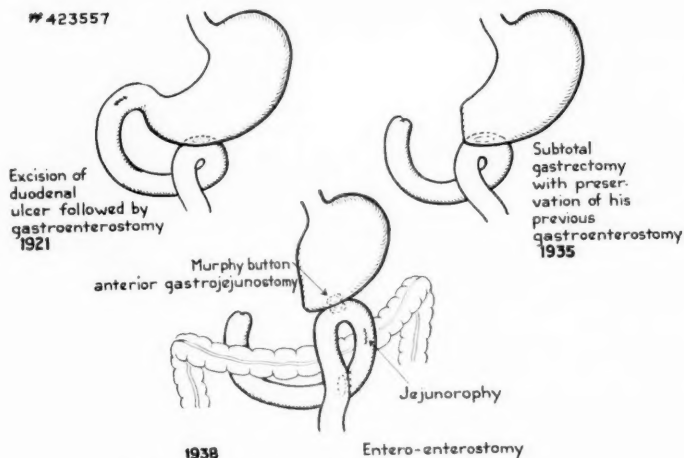
## GASTROJEJUNAL ULCERATION

elevated to 80 per cent. Gastrosocopy on two occasions revealed an ulcer on the gastric side of the posterior lip of the gastro-enteric stoma. Roentgenologic examination failed to reveal evidence of a gastrojejunal ulcer.

Operation was performed on May 26, 1938, under avertin and cyclopropane. The omentum was adherent to the previous scar, and the stomach was bound to the under



CASE 7.—Roentgenograms taken in 1934 showing duodenal and gastrojejunal ulcers.



CASE 7.—Schematic review of operative procedures.

surface of the liver by dense adhesions. The transverse colon was finally brought into the wound, exposing the site of a no-loop, anteperistaltic, posterior gastro-enterostomy. The afferent loop of this was constricted by adhesions. Definite induration was felt in the posterior region of the stoma, evidently the site of a healed marginal ulcer. A secondary subtotal gastrectomy was performed removing 6 cm. of the lesser curvature and 13 cm. of the greater curvature of the stomach. The proximal end of the small gastric segment was then closed, and an anterior antecolic button gastro-enterostomy, with a suture entero-enterostomy was performed. Prior to this the jejunal opening had been closed by a transverse jejunorrhaphy.

Patient's recovery was uneventful. When last seen, February 14, 1940, he had gained materially in weight, had no further episodes of bleeding, and seemed quite well.

The removal of a gastric segment in a case of partial gastrectomy with a retrocolic anastomosis, complicated by gastrojejunal ulceration, is a difficult procedure. The mobilization of the ulcerated stoma from its attachment to the transverse colon, and occasionally the pancreas, must be carefully undertaken in order to avoid injury to the middle colic artery. A secondary radical subtotal gastrectomy of this type may, perforce, leave a segment of stomach so small that a suture gastro-enterostomy may be extremely difficult and often too time-consuming. In cases such as this, we have found the use of either the Murphy button or its modifications invaluable. The site of the jejunum chosen for the anastomosis, as a rule, was distal to the area of jejunal resection and its union to the stomach was made anterior to the colon. The button anastomosis was further secured by interrupted Lembert sutures. A button gastrojejunostomy in a high resection, as a rule, produced a sharp angulation between the afferent and efferent jejunal loops. In spite of the fact that a jejunojejunostomy in the average subtotal gastrectomy is obviously a poor procedure because it deprives the stomach of the beneficial effects of full duodenal regurgitation, we have employed it as a safety measure against a possible acute jejunal obstruction. Any obstruction involving the loop of bowel which has been recently sutured will invariably result in a dehiscence, with an ensuing fatal peritonitis.

(6) *Gastrojejunal Ulceration Following Radical Subtotal Gastrectomy.*—Recurrent gastrojejunal ulcers following a radical subtotal gastrectomy of the Billroth II-type unfortunately occasionally occur. These patients represent an unfortunate group in which regardless of the extent of gastric resection, in spite of the full regurgitation of the duodenal contents, and the rapidity of the emptying, unneutralized free hydrochloric acid is still present in the remaining stomach. This, together with the constitutional tendency of the mucous membrane, especially of the jejunum, to ulcerate in the presence of free hydrochloric acid, produce a combination against which present-day surgery appears powerless. Theoretically, in order to cure this condition, total gastrectomy is indicated. The operation of total gastrectomy combined with jejunal resection results in a mortality of staggering proportions. As a matter of fact, in our hands, the attempt to remove additional portions of the stomach just short of a total gastrectomy gave an exceedingly high mortality. Therefore, when courses of medical treatment have proven to be ineffective, we have tried several palliative procedures in this type of case. Theoretically, with the chemical phase of gastric secretion eliminated by resection of the pylorus and antrum, the psychic phase of gastric secretion should be lessened by a vagotomy. Naturally, a vagotomy cannot be a complete one. In one case, in which a radical subtotal gastrectomy with exclusion was performed for massive duodenal ulceration, a gastrojejunal ulceration promptly took place. Inasmuch as this patient did not respond

## GASTROJEJUNAL ULCERATION

to medical treatment, a transthoracic, bilateral supradiaphragmatic vagotomy was performed, dividing the main anterior and posterior vagus trunks, *i.e.*, about 60 per cent of the vagus nerve supply to the stomach. There was little reduction in acid values according to the insulin test meal, and very little improvement clinically (Case 8).

**Case 8.**—History No. 420331: K. W., age 36. Admitted October 24, 1940. Discharged November 16, 1940.

1938—Prepyloric exclusion for duodenal ulcer and subtotal gastrectomy, with Hofmeister retrocolic gastrojejunostomy.



CASE 8.—Roentgenogram showing jejunal ulcer following subtotal gastrectomy, with exclusion of duodenal ulcer.

1939—Transthoracic bilateral vagotomy.

1940—Thoracotomy for empyema.

This is the readmission of a patient who, on a previous occasion, was treated medically for duodenal ulcer and who, because of intractability of pain in March, 1938, had a prepyloric exclusion of a massive penetrating duodenal ulcer and subtotal gastrectomy, with a Hofmeister retrocolic gastrojejunostomy, under spinal anesthesia.

He was readmitted again, within two months after discharge, for a jejunal ulcer, verified roentgenologically. He was then referred to the genito-urinary clinic for medical treatment.

In May, 1939, he was again admitted to the hospital for treatment, at which time he had a free acid of 40 and a total acidity of 48 units. Because of extreme loss of weight, and the intractability of his symptoms, due to the presence of a large gastro-jejunal ulcer, a transthoracic, supradiaphragmatic, bilateral vagotomy was performed, November 18, 1939.

Postoperatively, he developed a pleural effusion, which was aspirated and found to be negative on culture. Pre- and postoperative insulin test meal for vagus function showed no essential difference.

On October 30, 1940, he was admitted to the service of Doctor Neuhof for an empyema thoracis, for which a thoracotomy, in the left paravertebral region, was performed. When last seen, December 17, 1940, the empyema cavity was rapidly closing, and the gastric symptoms seemed somewhat more under control.

In another case of massive jejunal ulceration following radical subtotal gastrectomy, an infradiaphragmatic, anterior vagotomy combined with a



CASE 9.—Roentgenogram showing jejunal ulcer following subtotal gastrectomy for duodenal ulcer.

Stirling-type of procedure and a jejunostomy were performed. There was no reduction in the amount of free hydrochloric acid. The patient was, however, improved temporarily by a drip of amphogel. The present outlook in this type of case appears quite dismal (Case 9).

**Case 9.**—History No. 436115: L. R., age 44. Admitted October 21, 1940. Discharged February 9, 1941.

1939—Subtotal gastrectomy, with posterior retrocolic Murphy button gastrojejunostomy, for bleeding duodenal ulcer.

## GASTROJEJUNAL ULCERATION

1940—Anterior vagotomy, Stirling procedure, and jejunostomy for gastrojejunal ulcer.

A subtotal gastrectomy, with a posterior retrocolic Murphy button gastrojejunostomy was performed for a penetrating and bleeding duodenal ulcer in May, 1939, as an emergency procedure. The postoperative course was stormy and was complicated by an operative bronchopneumonia; a duodenal leak resulting in the formation of an intra-abdominal abscess, which was subsequently drained.

Patient was readmitted to the Medical Service on four separate occasions for recurrences of postprandial abdominal pain. In August, 1940, a gastro-intestinal series revealed a gastrojejunal ulcer. Because of the fact that this patient was not relieved by medical treatment, and had lost persistently in weight, he was reexplored, at which time a large gastrojejunal ulcer was found in the posterior wall of the gastrojejunostomy. The segment of stomach which remained was so small that no further resection was possible. Because of the marked ulceration in the jejunum, no jejunal resection was performed. Therefore, an anterior vagotomy and a Stirling-type of procedure were performed in the region of the cardia. A Witzel jejunostomy was done for alimentation. He developed a severe bilateral bronchopneumonia which almost caused his death. Although he was kept under observation for several months, there was no improvement clinically, despite the vagotomy, gastric mucin, injections of activin and paravertebral block of the nerve roots D9 and D10. The jejunal alimentation gave no relief. There was no clinical improvement in the condition of the patient. The insulin vagus test meals which were done pre- and postoperatively showed no difference. He was discharged finally to a convalescent home.

(7) *Gastrojejunocolic Fistulae*.—One of the most serious complications of a jejunal ulcer is its penetration into the transverse colon. The fistula generally connects the efferent jejunal loop and the colon, and lies quite close to the gastro-enterostomy stoma. It is a condition requiring immediate surgical treatment to prevent rapid death from inanition. There have been many operations which have been devised for the surgical treatment of gastrojejunocolic fistula, depending upon the extent of the pathologic condition present at the time of operation. We are convinced that separation of the gastro-enterostomy, with or without colonic resection, is an inadequate procedure. The aim of any operation employed, therefore, should be the elimination of the jejunal ulcer by excision, the restoration of colonic continuity, and the performance, either simultaneously or eventually, of an adequate gastrectomy. In 1939, Pfeiffer<sup>2</sup> suggested a preliminary ascending colostomy with the function of a spur, insuring a complete diversion of the fecal current. He felt that the inflammatory exudate present about these lesions would be diminished by this procedure, making any subsequent surgery much simpler. Having seen the benefits of jejunostomy in diminishing the massive exudates about a gastrojejunal penetration, we were convinced of the logic of employing a preliminary colostomy in large gastrojejunocolic fistulae in patients in poor condition. In patients in which the lesion is not extensive, the operation may be performed either in one or two stages (Case 10).

**Case 10.**—History No. 426675: N. W., age 49.

1935—Retrocolic posterior gastro-enterostomy for duodenal ulcer with pyloric stenosis.

1938—Ascending colostomy with spur for gastrojejunocolic fistula. (May)



1938—Subtotal gastrectomy, with antecolic terminolateral gastrojejunostomy and jejunal resection, with jejunojejunostomy for jejunal ulcer. (July)

1938—Closure of colostomy.

This patient was first admitted to the hospital January 7, 1935. He gave a nine-year history of intermittent attacks of epigastric, postprandial burning pain associated with nausea, occasional vomiting, eructations, and pyrosis. One week before admission, a gastro-intestinal series was done, and a penetrating duodenal ulcer, with a large gastric residue after five hours, was found. On January 12, 1935, under spinal anesthesia, through a median epigastric incision, a retrocolic, posterior no-loop gastro-enterostomy was performed for chronic duodenal ulcer producing a partial pyloric obstruction. The postoperative course was uneventful, and he was discharged 12 days after operation. The patient felt fairly well until three months before his second admission, when he again began to have frequent bowel movements accompanied by the belching of fecal tasting gas. He had lost ten pounds during this period. Barium enema revealed the presence of a gastrojejunocolic fistula.

He was readmitted to the hospital April 13, 1938. He appeared to be well-nourished. He belched frequently, with a feculent odor apparent on the breath. There was a small incisional hernia at the previous operative site. Hemoglobin 70 per cent. Urine clear. Blood chemistry normal. Electrocardiogram negative. A night Rehfuess test meal revealed a free acid of 80, and a total acid of 128 units. When a methylene blue enema was administered to the patient, the dye appeared 20 minutes later through a gastric Levin tube, establishing the presence of a gastrojejunocolic fistula. On May 6, 1938, under spinal anesthesia, and through an upper right rectus muscle-splitting incision, the ascending colon was mobilized. Crushing clamps were applied to the midportion of the colon, which was exteriorized, while the distal and proximal limbs were united to form a spur. The colon was divided between the clamps. The proximal colonic loop was opened 24 hours after operation, and the clamps were removed on the sixth day. Almost immediately, the patient noted that his breath was no longer fecal. At the time of discharge, the entire fecal stream was side-tracked and draining well through the proximal colostomy. The distal colonic segment, however, was still in communication with the stomach, as was evidenced by the appearance of methylene blue in the gastric Levin tube 20 minutes after the dye had been administered in an enema. He was discharged May 17, 1938.

The patient reentered the hospital July 8, 1938. He was asymptomatic and had gained about 18 pounds. A gastro-intestinal series showed evidence of a previous gastro-enterostomy. The barium mixture passed through the stoma which was tender and irregular; within the jejunum about two inches from the stoma, a large ulcer pocket, one inch in diameter, was observed. There was no evidence of a gastrojejunocolic fistula. A barium enema, injected through the colostomy, showed irregularity of the midportion of the transverse colon but no communication between the colon and stomach. On July 16, 1938, under anesthesia, the scar of the previous median epigastric incision was excised. In the region of the previous gastro-enterostomy there was a hard, inflammatory mass about the size of a lemon, which included the stomach, colon, and jejunum. About 12 inches from the duodenojejunal angle, the efferent jejunum was found to be the seat of a definite ulceration almost opposite the neostomy. The fistula in the colon had evidently healed and was replaced by hard, fibrous, indurated connective tissue. The stomach itself was dilated to about twice its normal size, and this was apparently caused by a stenosis at the duodenum due to a healed duodenal ulcer. A partial jejunectomy, with end-to-end jejunojejunostomy, for a jejunal ulcer, and a subtotal gastrectomy with a Hofmeister antecolic gastro-enterostomy, for healed ulcer of the duodenum, with pyloric stenosis, was performed.

After a moderate febrile reaction, and some gastric regurgitation, the patient did well. A spur-crusher was applied to the colostomy two weeks after operation, and two weeks later, an extraperitoneal closure of the colostomy was performed, under ethylene,

## GASTROJEJUNAL ULCERATION

by Dr. P. Klingenstein. When last seen, March 1, 1941, the patient looked and felt well. He had gained 25 pounds since his operation.

### SUMMARY

The pathology, symptomatology, physical, roentgenographic, gastroscopic, and chemical findings in cases of gastrojejunal ulceration following gastro-enterostomy, partial, and subtotal gastrectomy are reviewed. The medical treatment and surgical indications are discussed.

The surgical management of gastrojejunal ulceration and its complications depend upon the pathology present at the time of operation. Cases are arbitrarily divided into: (1) Perforation of acute gastrojejunal ulcers following gastro-enterostomy; (2) resectable gastrojejunal ulcers following gastro-enterostomy; (3) massive gastrojejunal ulcers following gastro-enterostomy; (4) cicatrized gastrojejunal ulcers following gastro-enterostomy; (5) resectable gastrojejunal ulcers following partial gastrectomy; (6) resectable gastrojejunal ulcers following subtotal gastrectomy; and (7) gastrojejunocolic fistula.

A detailed discussion of the surgical problems involved in each group with case presentations are given.

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- <sup>2</sup> Pfeiffer, D. B., and Kent, E. M.: *ANNALS OF SURGERY*, **110**, 659, October, 1939.

## SURGICAL MANAGEMENT OF CARCINOMA OF THE AMPULLA OF VATER AND OF THE PERIAMPULLARY PORTION OF THE DUODENUM\*

VERNE C. HUNT, M.D.

LOS ANGELES, CALIF.

IN 1935, Whipple, Parsons, and Mullins presented a paper before this Association in which they directed attention to the problems involved in the surgical treatment of carcinoma of the ampulla of Vater and of the periampullary portion of the duodenum. They described and illustrated a surgical procedure performed in two stages which embraces the fundamental principles of cancer surgery in general, *i.e.*, the excision of tissue *en bloc*, wide of the growth, which stimulated anew an endeavor to surgically extirpate neoplastic disease in that situation.

Characteristically, patients in whom neoplastic obstruction of the terminal portion of the common duct occurs, lose weight rapidly through retention of bile and the loss of external pancreatic secretion, to become subjects for surgical procedures in which the risk of operation is far greater than in operations employed for the relief of temporary, intermittent, or incomplete obstruction of the common duct resulting from benign disease. Even though the advantages of drainage and decompression of the biliary tract preliminary to any radical surgical procedure for the extirpation of neoplastic disease in the ampullary region have long been recognized, the risk of such operations has in the past been great (30 to 70 per cent).

Since 1898, when Halsted successfully performed the first radical operation for carcinoma of the ampulla of Vater through resection of the duodenum with end-to-end anastomosis and reimplantation of the common and pancreatic ducts into the duodenum, less than 125 instances have been recorded in which radical excision of malignant disease in this situation has been accomplished. Should one rely solely upon the number of cases in which surgical extirpation of a malignant lesion in the periampullary region has been undertaken, he would be inclined to the opinion that malignant disease in this situation is exceedingly uncommon. In searching the literature for recorded instances of surgical excision and radical resection of neoplastic disease in the ampullary region, a startling number of cases were encountered in which the diagnosis was made at necropsy, which more often than not disclosed an entirely localized operable lesion. In 1913, Outerbridge collected 110 cases of carcinoma of the ampulla of Vater and in only 22 of those had a resection of the ampulla been performed. In 1939, Lieber, Stewart, and Lund collected 399 cases of carcinoma of the ampulla of Vater which, with the exception of a few cases that were not available to them, represented all of the cases reported in the literature.

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\*Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

Upcott, Pallin, Einhorn and Stetten, Busch, Fulde, Muller and Rode-maker, among others, have presented extensive reviews of this subject. In 1927, however, Cohen and Colp provided the most complete collection of 58 cases in which radical operation for carcinoma of the ampulla of Vater had been performed during the period from 1898 to 1925. In 1934, reporting a case which had been successfully operated upon, Hunt and Budd collected 17 additional cases, which added to those of Cohen and Colp, provided a collective review of 76 cases. In 1935, Whipple, Parsons, and Mullins reported three cases of their own and added 19 cases from the literature since the report of Cohen and Colp. In a late collective review by Kafka, 115 cases are listed in which operation had been performed. I have recently collected from the literature and through personal communication 32 cases (abstracts appended) which, with those here recorded and added to those collected by Cohen and Colp, Whipple, Parsons and Mullins, and Hunt and Budd, provide 124 cases for review (Table I).

Four cases are herewith reported in which radical operation was successfully performed for carcinoma of the ampulla of Vater and periampullary region of the duodenum. Case 1 was reported before the Western Surgical Association in December, 1934, and was recorded in *Surgery, Gynecology, and Obstetrics* in November, 1935. The case is here presented in abstract form in order that the subsequent course, ultimate result, and necropsy findings may be made a matter of record.

#### CASE REPORTS

**Case 1.**—St. Vincent's Hospital, No. 3047-34: A woman, age 54, on August 15, 1934, gave a history of epigastric distress of three weeks' duration, with progressive jaundice. There had never been any acute pain or chills, but there had been a daily temperature of 100° F. A weight loss of ten pounds had occurred. At the time of examination, the patient was poorly nourished, weighed 98 pounds and was deeply jaundiced. General physical examination was essentially negative except for the presence of a large cystic mass occupying the entire upper left quadrant of the abdomen, which, upon subsequent investigation, proved to be a huge hydronephrotic left kidney. Apart from a secondary anemia, laboratory data, as detailed in a previous report, were essentially negative. A preoperative diagnosis of obstructive jaundice, probably due to carcinoma of the head of the pancreas was made.

**Operation.**—(Hunt): August 17, 1934: Transduodenal cautery excision of the ampulla of Vater with reimplantation of the common duct and duct of Wirsung into the posterior wall of the duodenum and external drainage of the common duct. The gall-bladder was greatly distended and the common duct was dilated to about 2.5 cm. in diameter, and both of these structures contained colorless, mucoid material under pressure. An incision in the anterior wall of the duodenum exposed a nonulcerating tumor of the ampulla, projecting into the lumen of the duodenum (Fig. 1). A wide transduodenal cautery excision of the tumor was made, dividing the dilated common and pancreatic ducts (Figs. 2 and 3). The mesial edges of the common duct and the duct of Wirsung were sutured together and the circumferential edge of each duct was sutured to the mucosa of the posterior wall of the duodenum (Fig. 4). Temporary external drainage of the common duct was established by an ordinary catheter. *Pathologic Diagnosis:* Papillary adenocarcinoma primary in the ampulla of Vater, Grade III (Fig. 5).

TABLE I

124 CASES OF RADICAL OPERATION FOR CARCINOMA OF THE PERIAMPULLARY REGION OF THE DUODENUM  
FROM 1898 TO 1941

Year	Surgeon	Sex	Age	Operation	Result
1898	Halsted*	M.	60	Resection of duodenum (circular suture) (end-to-end) reimplantation of choledochus and pancreatic ducts and cholecystostomy	Death 7 mos. after resection from recurrence
1899	Riedel*	F.	50	Transduodenal excision	Died from operative shock same day
1900	W. J. Mayo*	F.	59	Cholecystostomy. 3 mos. later transduodenal excision with the cautery. 18 mos. later cholecystoduodenostomy because of recurrence	Died after operation for recurrence from shock
1901	Czerny*	M.	66	Transduodenal excision and cholecystostomy	Died after 5 days from retroduodenal phlegmon
1901	Rixford*	F.	33	Cholecystostomy and 1 mo. later transduodenal excision. 8 mos. later cholecysto-enterostomy because of recurrence	Died 4 mos. after the last operation from recurrence
1903	Koerte*	F.	44	Transduodenal excision and choledochopancreaticoduodenostomy. Drainage of hepatic and pancreatic ducts and gallbladder	Died 8 days after operation
1904	Mayo Robson*	M.	33	Resection of duodenum and pylorus; suture of duodenum and pylorus; cholecystostomy	Died few days after operation
1904	Koerte*	F.	53	Transduodenal plastic on papilla (excision of stricture). Drainage of pancreatic and hepatic ducts, and cholecystostomy. 1 3/4 yrs. later, resection of duodenum (circular and end-to-end suture), common and pancreatic ducts cut through, sutured together and reimplanted into posterior duodenal wall	Operative recovery. Patient well for 1 1/2 yrs., then jaundice returned. Died third day after operation
1904	Arnsperger*	F.	43	Transduodenal excision and insertion of choledochus. Drainage of hepatic duct	Died 2 days after operation from hemorrhage
1905	Koerte*	F.	47	Transduodenal excision and common duct reimplanted into duodenum	Operative recovery. Alive 22 yrs. after operation
1905	Verroogen*	F.	33	Transduodenal excision	Died 11 days after operation from hematemesis and duodenal leakage
1905	Cordua*	F.	41	Transduodenal excision, Cholecystectomy and gastro-enterostomy	Operative recovery. Died 1 yr. later from recurrence
1905	Mayo*	M.	49	Retroduodenal papillectomy, choledochoduodenostomy	Died after 8 wks.
1908	Morian*	F.	42	Transduodenal excision, cholecystojejunostomy	Operative recovery. Died 2 1/2 yrs. later from recurrence
1908	Cuneo*	M.	59	Transduodenal excision, reinsertion of choledochus, gastro-enterostomy	Died 4 days after operation
1908	Navarro*	M.	60	Transduodenal excision, reinsertion of choledochus and pancreaticus	Operative recovery. Alive 2 yrs. after operation. No recurrence
1909	Kausch*	M.	49	Cholecystojejunostomy. 2 mos. later resection of duodenum and part of pancreas. Pancreaticoduodenostomy and gastro-enterostomy	Operative recovery. Died 3/4 yr. later from cholangitis
1910	Stein*	?	?	Duodenotomy. Soft, friable papillary mass surrounding papilla curetted away	Operative recovery. Patient alive 7 mos. later

\* Collected by Cohen and Colp in 1927.



# PERIAMPULLARY CARCINOMA

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1910	Kraske*	F.	60	Transduodenal excision. Reinsertion of choledochus	Operative recovery. Severe hemorrhage first day postoperative After 23 mos. developed slight jaundice, probably from a recurrence
1910	Kelly*	F.	45	Transduodenal excision. Reimplantation of choledochus	Operative recovery. Patient alive 9 yrs. after operation
1910	Kerr	M.	52	Transduodenal excision with reimplantation common duct and duct of Wirsung	Lived 3 yrs. (Kafka)
1911	Hotz*	F.	61	Retroduodenal excision and gastro-enterostomy	Operative recovery
1911	Slaymer*	M.	48	Retroduodenal excision, reinsertion of choledochus and pancreaticus. Choledochostomy and jejunostomy	Died after 3 days from cholemic hemorrhages
1912	Hartman*	?	?	Transduodenal excision with reimplantation of choledochus	Operative recovery. Recurrence 2 mos. after operation
1912	Upcott*	M.	65	Transduodenal excision and reinsertion of choledochus. Cholecystostomy	Operative recovery. Treated later with radium because nodes suspected of being malignant were not removed
1912	Oppenheimer*	F.	63	Choledochotomy at first then resection of entire choledochus and surrounding indurated area. Hepatic duct sutured to duodenum. Cholecystectomy. Stump of pancreatic duct, which had been cut through, sunk into duodenal wall	Operative recovery. Died 1 yr. later from recurrence in liver
1913	Hirschel*	F.	47	Circular resection of the duodenum. End-to-end suture. Choledochoduodenostomy with tube. Resection of part of pancreas and pancreaticoduodenostomy and gastro-enterostomy	Operative recovery. Died 1 yr. later from recurrence
1913	Algave*	?	?	Transduodenal excision. Choledochostomy	Died 8 days after operation from cholemia and anuria
1913	Hartman*	?	?	Transduodenal excision. Reimplantation of choledochus	Operative recovery. Patient alive 18 mos. after operation
1913	Clermont*	?	?	Transduodenal excision	Died night of operation from hemorrhage
1913	Kleinschmidt*	F.	51	Cholecystectomy. Transduodenal excision	Died eighth day from peritonitis
1914	Docq-VanPsever*	?	?	Transduodenal excision	Operative recovery
1914	Docq-VanPsever*	?	?	Transduodenal excision	Died fourth day from hemorrhage
1914	Wiede*	?	?	Transduodenal excision	Operative recovery
1914	Wiede*	?	?	Transduodenal excision	Died from cholemic hemorrhages. At postmortem, no metastases found
1916	Akerblom*	F.	72	Transduodenal excision	Died after 8 days from cholemic hemorrhages
1917	Akerblom*	?	?	Transduodenal excision	Died after 2 days from pancreatic hemorrhage

\* Collected by Cohen and Colp in 1927.

|| Collected by Hunt in 1941.

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1918	Anschutz*	F.	36	Transduodenal excision and reimplantation of choledochus. Pylorus occluded and posterior gastro-enterostomy. Cholecystostomy for 8 days	Operative recovery. Gained 30 lbs. in 4 mos.
1919	Lundblad*	F.	59	Transduodenal excision	Died after 3 days from cholemic hemorrhages
1919	Oliani*	?	?	Transduodenal excision and reimplantation of choledochus. Cholecystectomy with drainage	Operative recovery. Patient alive 4 yrs. later
1919	Arnsperger*	F.	50	Transduodenal excision and reimplantation of choledochus. Hepatic drainage	Operative recovery. Patient died 6 mos. later from metastases
1919	Schüssler	M.	43	Resection of duodenum with reimplantation of common duct and duct of Wirsung	Death ninth day from hemorrhage
1919	Schüssler	F.	34	Transduodenal excision and reimplantation of common duct	Recovery. Good health at end of 4 mos.
1920	Blad	F.	62	Transduodenal excision and reimplantation of common duct	Recovery. Good health at end of 16 mos.
1920	Brentano*	M.	45	Transduodenal excision	Operative recovery. Nine mos. later local recurrence
1921	Propping*	F.	17	Transduodenal excision and reimplantation of pancreatic and choledochus ducts	Operative recovery. Alive 1 yr. later and gained 30 lbs.
1921	Kleinschmidt*	F.	41	Transduodenal excision. Drainage of duct of Wirsung	Operative recovery. Well 7 mos. later
1922	Renshaw*	?	?	Choledochotomy, transduodenal excision (knife and cautery), cholecystoduodenostomy	Died 9 days after operation
1922	Bruett*	F.	59	Cholecystectomy. Transduodenal excision and reimplantation of choledochus and duct of Wirsung	Died 2 days after operation from peritonitis
1922	Bruett*	M.	50	Transduodenal excision and reimplantation of choledochus and duct of Wirsung	Operative recovery. Died $\frac{3}{4}$ yr. later
1922	Bruett*	M.	43	Transduodenal excision and reimplantation of choledochus and pancreatic duct	Operative recovery. Alive 6 mos. later
1923	Tenani*	?	?	First operation: Duodenotomy, posterior gastro-enterostomy; division of choledochus with implantation of proximal end into efferent duodenal segment. Suture of duodenum and closure of abdomen without drainage. Second operation (one mo. later): Duodenum mobilized and descending part resected. Diseased head of pancreas removed and pancreatic stump sutured into efferent duodenal segment and suture line protected with peritoneum	Postoperative reaction severe. Patient free from recurrence 3 yrs. after operation
1922	Judd†	M.	55	First stage: Cholecystostomy. Second stage: Transduodenal excision and choledochoduodenostomy	Death 2 days after operation
1923	Dalla Valle*	?	?	Transduodenal excision and reimplantation of choledochus	Died 3 days after operation

\* Collected by Cohen and Colp in 1927.

|| Collected by Hunt in 1941.

# PERIAMPULLARY CARCINOMA

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1923	Pozzi*	?	?	Duodenotomy. Excision of papilla with reimplantation of duct of Wirsung and choledochus. Cholecystogastrostomy	Operative recovery.
1923	Pozzi*	?	?	Choledochotomy. Transduodenal excision of papilla with reimplantation of choledochus and Wirsung. Cholecystogastrostomy	Died 6 days after operation from peritonitis
1923	Pozzi*	?	?	Duodenotomy. Excision of papilla with reimplantation of choledochus and duct of Wirsung	Operative recovery. Patient alive 3 yrs. after operation
1923	Beer*	M.	34	Transduodenal excision. Cholecystogastrostomy	Died in 10 hrs. from shock
1924	Moschcowitz*	F.	54	Choledochotomy. Transduodenal excision. Drainage to suture lines of common duct and duodenum	Died 5 days after operation from hemorrhage
1924	Tomaschewitch*	?	?	Transduodenal excision	Death 11 days after operation from duodenal fistula
1924	Brenner	M.	58	Transduodenal excision	Recovery. Subsequent course?
1925	Gohrbrandt*	M.	?	Transduodenal excision and reimplantation of common bile and pancreatic ducts	Operative recovery. Alive 4 mos. later
1925	Muller*	M.	52	Transduodenal excision	Operative recovery. Death from metastases 4 yrs. and 8 mos. after operation
1925	Cohen*	F.	44	Choledochotomy. Transduodenal excision. Cholecystostomy and drainage	Operative recovery. Died 11 mos. later from metastases
1925	Hansen†	M.	44	One-stage transduodenal excision and cholecystostomy	Operative recovery. Recurrence and death in 18 mos.
1925	Konjetzny†	M.	55	One-stage combined retroduodenal and transduodenal excision; reimplantation of common duct and duct of Wirsung	Recovery
1925	Homans‡	?	?	One-stage transduodenal cautery excision	Well after several years
1925	Cabot††	M.	35	One-stage transduodenal excision and reimplantation of common duct	Well after 8 yrs.
1926	Eiselsberg	?	?	Transduodenal excision	Recovery. Subsequent course?
1926	Eiselsberg	?	?	Transduodenal excision	Death third day from hemorrhage
1926	Lagos and Dominguez	M.	41	Transduodenal excision and reimplantation of common duct	Death 16 hrs. after operation; hemorrhage
1927	Clart‡	?	?	One-stage transduodenal excision, with reimplantation of common duct and the duct of Wirsung	Living and well 5 yrs. after operation
1927	Fulde‡	M.	46	One-stage transduodenal excision, with reimplantation of common duct and the duct of Wirsung	Living and well 2 yrs. after operation
1928	Collert‡	M.	64	One-stage transduodenal excision, with reimplantation of common duct	Death on fourth day (cholemia)
1928	Busch†	M.	53	First stage: Cholecystostomy. Second stage: Transduodenal excision, with reimplantation of common duct and duct of Wirsung	Well after 1 yr.

\* Collected by Cohen and Colp in 1927.

† Collected by Hunt in 1934.

‡ Collected by Whipple, Parsons, and Mullins in 1935.

|| Collected by Hunt in 1941.

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1928	Llambias†	M.	42	One-stage transduodenal excision with reimplantation of the common duct and duct of Wirsung; cholecystectomy and choledochostomy	Recovery
1928	Del Valle‡	M.	42	One-stage transduodenal excision, cholecystectomy and choledochostomy	Recovery
1929	Klinkert‡	M.	53	First stage: Cholecystojejunostomy. Second stage: Transduodenal excision and gastro-enterostomy	Operative recovery. Death in 3 mos. from liver metastases
	Pollet‡	?	?	First stage: Cholecystojejunostomy. Second stage: Transduodenal excision with reimplantation of common duct and duct of Wirsung	Recovery
1929	Denks†	F.	31	One-stage resection of duodenum and part of head of pancreas; end-to-end anastomosis of duodenum to pylorus; reimplantation of common duct into stomach	Death on third day. No metastases at autopsy
1929	Denks†	M.	?	One-stage transduodenal excision and reimplantation of common duct and duct of Wirsung; choledochostomy	Death on sixth day
1930	Bengolea‡	F.	37	One-stage excision through choledochotomy opening and choledochostomy	Recovery. Secondary operation 3 mos. later from recurring jaundice; metastases
1931	Walters††	M.	50	One-stage transduodenal excision, with reimplantation of common duct into duodenum	Operative recovery
1931	Pemberton††	M.	44	One-stage transduodenal excision, with reimplantation of pancreatic duct into duodenum; choledochoduodenostomy	Recurrence and death 2 yrs. after operation
1931	De Beule	?	?	Transduodenal excision and reimplantation of common duct	Recovery. Metastases to liver within few mos.
1931	De Beule	?	?	Transduodenal excision and reimplantation of common duct	Lived 3 yrs.; death from influenza
1931	De Beule	?	?	Resection of duodenum and end-to-end anastomosis of duodenum; cholecystogastrostomy	Death soon after operation
1932	Judd††	M.	38	First stage: Cholecystostomy and choledochostomy. Second stage: 1 mo. later transduodenal excision	Recurrence 9 mos. after operation requiring cholecystogastrostomy. 7 mos. later gastro-enterostomy; lived 2½ yrs.
1933	Potter††	F.	57	One-stage transduodenal excision with reimplantation of common duct and the duct of Wirsung	Operative recovery. Death 6 mos. later; metastases?
1933	Lauwers††	M.	51	One-stage transduodenal cautery excision and cholecystojejunostomy	Living and well 3 yrs. 10 mos. after operation
1933	Lauwers††	M.	52	One-stage transduodenal excision with reimplantation of duct of Wirsung; cholecystojejunostomy	Well 9 mos. after operation
1934	Snyder and Lium	M.	48	First stage: Cholecystoduodenostomy and drainage of common duct. Second stage: Transduodenal excision, with reimplantation duct of Wirsung and external catheter drainage of duct of Wirsung	Recovery. Subsequent course?

† Collected by Hunt in 1934.

‡ Collected by Whipple, Parsons, and Mullins in 1935.

|| Collected by Hunt in 1941.

# PERIAMPULLARY CARCINOMA

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1934	Santero†	M.	50	One-stage transduodenal excision	Recurrence 17 mos. after operation. Second radical excision at this time. Death 22 mos. after first excision
1934	Santero†	F.	72	One-stage transduodenal excision	Recurrence 4 mos. later necessitating palliative operation. Death 19 mos. after first operation
1934	Hunt† (Case 1)	F.	54	One-stage transduodenal excision, with reimplantation of common duct and the duct of Wirsung; choledochostomy	Lived 25 mos.; death from retroperitoneal, mediastinal metastases
1935	Whipple‡	F.	60	First stage: Cholecystostomy and choledochoduodenostomy. Second stage: Transduodenal excision and excision of part of head of the pancreas with pancreaticoduodenostomy	Death 36 hrs. after operation from duodenal leakage
1935	Parsons‡	M.	53	First stage: Cholecystogastrostomy. Second stage: Resection of duodenum and head of pancreas with closure of pancreatic stump; end-to-end anastomosis of duodenum. Third operation 8 days later: Anterior gastro-enterostomy and entero-enterostomy	Death in 8 mos. of cholangitis
1935	Whipple‡	M.	49	First stage: Gastro-enterostomy, ligation and division of common duct, and cholecystogastrostomy. Second stage: Resection of duodenum and head of pancreas, with closure of pancreatic stump	Recovery. Death after 28 mos. of metastases to liver
1935	Janes‡	M.	?	First stage: Cholecystogastrostomy. Second stage: (3 wks. later) Resection duodenum and adjacent pancreas; closure pancreatic stump; ligation of common duct; and gastro-enterostomy	Death fifth postoperative day of pneumonia
1935	Kafka	M.	52	Transduodenal excision and reimplantation of common duct and duct of Wirsung	Well 22 mos. after operation. Death of unknown cause 2 yrs. after operation
1935	Nemenyi	M.	42	Resection of duodenum and part of head of pancreas; pancreaticoduodenostomy; pylorojejunostomy and jejunojejunostomy	Well at end 16 mos., having regained nearly all weight
1936	Bumm   (Geisthövel)	M.	54	Transduodenal excision and reimplantation of common duct and duct of Wirsung; cholecystoduodenostomy	Six mos. after operation well and gained 22 lbs.
1936	Orator	F.	48	Whipple operation, first-stage; cholecystogastrostomy and posterior gastro-enterostomy. Second-stage: Resection of duodenum and part of head of the pancreas	Pancreatic fistula. 3 mos. after operation jejunostomy was provided to receive external pancreatic fistula
1936	Hyde and Young	F.	76	Transduodenal excision and reimplantation of common duct and duct of Wirsung; choledochostomy	Well at end of 3 yrs.

† Collected by Hunt in 1934.

‡ Collected by Whipple, Parsons, and Mullins in 1935.

|| Collected by Hunt in 1941.



TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1936	Hollenberg§	F.	45	Two-stage radical operation of resection of the duodenum and head of the pancreas	Pancreatic fistula persisted for 8 to 9 mos. Following spontaneous closure of fistula excellent health for 1½ yrs. Death of local recurrence 34 mos. after resection
1937	Hoffman and Pack	M.	58	First operation: T-tube drainage of common duct. Second operation: Transduodenal excision	Death 6 hrs. after operation from hemorrhage
1937	Mallet-Guy	F.	56	Transduodenal excision and choledochostomy	Recovery. Subsequent course?
1937	McCabe	M.	67	Transduodenal excision and reimplantation of common duct and duct of Wirsung; choledochostomy	Recovery after postoperative hemorrhage. Subsequent course?
1937	Brunschwig	F.	41	Transduodenal excision and reimplantation of common duct and duct of Wirsung	General condition good after 15 mos.
1937	Roscher	M.	55	First-stage: Cholecystogastrostomy. Second-stage: Resection of duodenum and part of head of pancreas; division and ligation common duct; implantation of common duct into jejunum; posterior gastro-enterostomy	Lived 5 mos. Death due to bronchopneumonia; metastases?
1937	Divis	F.	65	One-stage transduodenal excision with reimplantation of common duct and duct of Wirsung; cholecystoduodenostomy	Lived 1 yr.; cardiac death
	Janes§	?	?	Two-stage radical operation of resection of the duodenum and head of the pancreas	Death 2 wks. after operation from massive hemorrhage
	Schullinger§	?	?	Two-stage radical operation of resection of the duodenum and head of the pancreas	Death 2 wks. after resection of pneumonia
1938	Trout	M.	55	Whipple operation in one stage; cholecystojejunostomy; posterior gastro-enterostomy; division and ligation of common duct; resection of duodenum and part of head of pancreas <i>en bloc</i>	Death within a few hours after operation
1938	McNealy   (McNealy, River and Ragina)	F.	63	Transduodenal excision and reimplantation of common duct and duct of Wirsung	Recovered. Jaundice recurred in 16 mos. due to stricture at site of implantation; cholecystogastrostomy then performed. Living and well. 26 mos. after excision of tumor
1939	River	M.	55	Transduodenal excision and reimplantation of common duct; duct of Wirsung not seen	Jaundice recurred in 8 mos. due to stricture site of implantation; cholecystojejunostomy. Recovery.
1939	River	M.	55	Transduodenal excision and reimplantation of common duct and duct of Wirsung; cholecystostomy	Well 9 mos. after operation
1940	Maddock	M.	36	Resection of duodenum and end-to-end anastomosis of duodenum; reimplantation of common duct; cholecystectomy	Death on 14th day of peritonitis

|| Collected by Hunt in 1941.

§ Collected by Whipple in 1938.

# PERIAMPULLARY CARCINOMA

TABLE I (Continued)

Year	Surgeon	Sex	Age	Operation	Result
1940	Orr	M.	47	Whipple operation. First stage: Choledochogastrostomy and posterior gastro-enterostomy. Second stage: Division and ligation of common duct, resection of duodenum and part of head of the pancreas	Recovery. Small pancreatic fistula persisting 7 mos. after operation
1941	Ransom	M.	?	First stage: Cholecystojejunostomy, jejunojejunostomy; posterior gastro-enterostomy. Second stage: Resection of duodenum and part of head of the pancreas; ligation of common duct and duct of Wirsung	Recovery. Pancreatic fistula developed but was nearly closed on 25th postoperative day
1941	Whipple	M.	58	Two-stage operation; Whipple radical resection of duodenum and part of head of the pancreas	Well, free of jaundice; regained weight 15 mos. after operation
1941	Hunt   (Case 2)	F.	72	One-stage transduodenal excision and reimplantation common duct and duct of Wirsung, T-tube choledochostomy	Living 33 mos. after operation; no jaundice but with metastases
1941	Hunt   (Case 3)	F.	60	One-stage Whipple operation; cholecystogastrostomy; posterior gastro-enterostomy; resection of duodenum and part of head of the pancreas; division and ligation of common duct and duct of Wirsung	Recovered and in good health 1 yr. after operation. Pancreatic biliary fistula persisted until the 33rd postoperative day
1941	Hunt   (Case 4)	F.	43	First operation: Cholecystectomy and T-tube choledochostomy. Second stage: Total duodenectomy and cauterly excision of part of the head of the pancreas, jejuno-pancreatostomy, jejunocholedochostomy, and posterior gastro-enterostomy	Recovery. T-tube removed from common duct on 8th postoperative day; no external biliary drainage after 11th postoperative day

|| Collected by Hunt in 1941.

*Postoperative and Subsequent Course.*—After three days, some pigment appeared in the bile as it drained from the choledochostomy tube, and the pigment became of gross normal concentration by the eighth day. The tube was removed on the eighteenth day and the patient was dismissed from the hospital on the twenty-ninth postoperative day with the wound healed and her general condition good. Ten months after the operation the patient had gained 35 pounds, and was feeling very well except for symptoms referable to the previously noted huge left hydronephrotic kidney. On July 1, 1935, a left nephrectomy was performed.

At about October 1, 1935, or 14 months after the original operation, the patient developed some discomfort in the chest and vomited occasionally. Six months later considerable weight had been lost and difficulty in swallowing was experienced. Subsequent esophagoscopic examination revealed a stricture at the level of the arch of the aorta. There never was recurrence of jaundice, but the patient's decline continued and death occurred, September 9, 1936, nearly 25 months after excision of the tumor of the ampulla.

*Autopsy.*—Anatomic diagnosis: (1) Extensive carcinoma of the retroperitoneal tissues and the mediastinum secondary to carcinoma of the ampulla of Vater. (2) Marked stenosis of the esophagus, trachea, and aortic arch from neoplastic involvement of the superior mediastinum.

**Case 2.**—St. Vincent's Hospital, No. 3282-38: A woman, age 72, on May 13, 1938 stated that for 12 years she had had recurring attacks of upper abdominal pain, nausea

and vomiting. There was some jaundice for a few days following an attack of pain 12 years ago. Roentgenologic examination of the gallbladder was said to have visualized stones. Following the last severe attack of upper abdominal pain three weeks before

FIG. 1.



FIG. 2.

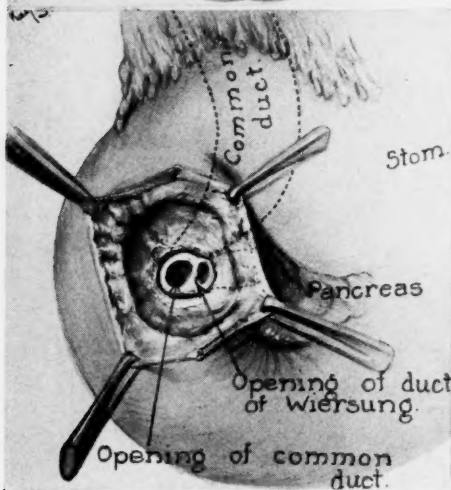
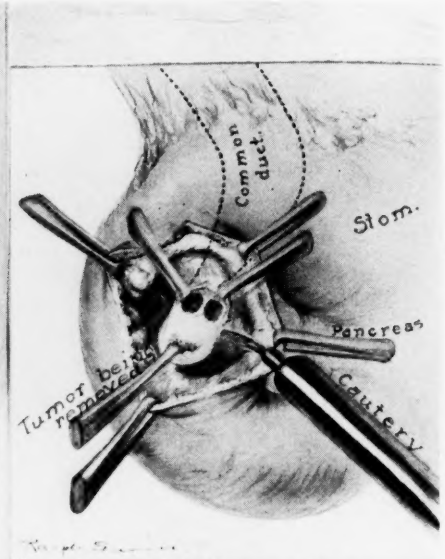


FIG. 3.

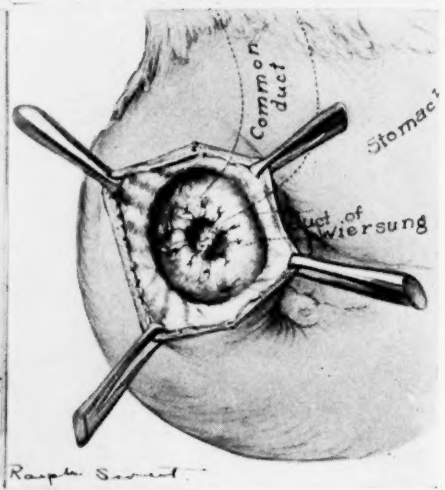


FIG. 4.

- FIG. 1.—Tumor of the ampulla of Vater visualized upon opening the duodenum (Case 1).  
 FIG. 2.—Transduodenal cautery excision of tumor—method employed in Cases 1 and 2.  
 FIG. 3.—Marked dilatation of the common and pancreatic ducts (Case 1).  
 FIG. 4.—Common and pancreatic ducts reimplanted into the posterior wall of the duodenum.

admission, the patient became moderately jaundiced and some jaundice persisted, with dark urine and clay-colored stools. The patient had lost 20 pounds in weight.

Upon examination, the patient was poorly nourished, weighed 84 pounds, and was moderately jaundiced. Blood pressure 170/90. The liver edge was palpable at the level of the umbilicus and was tender. The gallbladder was not palpable. General physical examination was otherwise essentially negative.

# PERIAMPULLARY CARCINOMA

*Laboratory Data.*—Uranalysis: Specific gravity 1.020, acid reaction, a trace of albumin, no sugar, and microscopic elements were absent with the exception of a few pus cells. The concentration of the hemoglobin was 13 Gm. per 100 cc. of blood (78 per cent), R.B.C. 3,820,000; W.B.C. 6,700, with a normal differential count; the bleeding time was

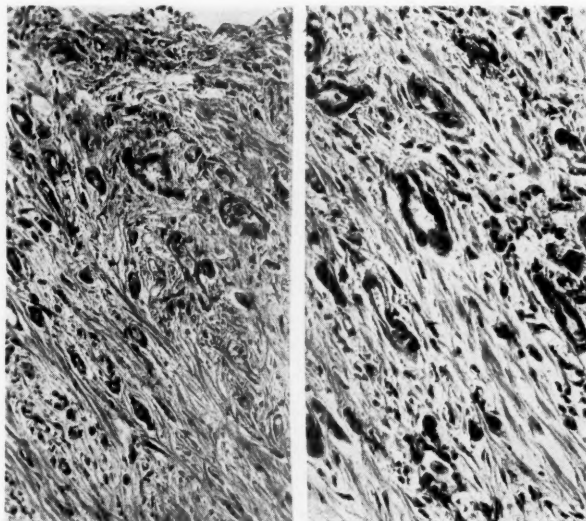


FIG. 5.—Photomicrograph of Case 1: Adenocarcinoma, Grade III (left  $\times 128$ ; right  $\times 245$ ).

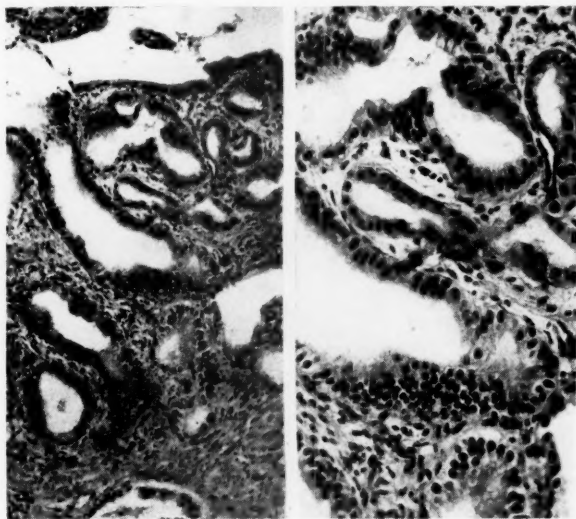


FIG. 6.—Photomicrograph of Case 2: Adenocarcinoma, Grade III (left  $\times 128$ ; right  $\times 245$ ).

two minutes and the coagulation time was five and one-half minutes. A diagnosis of common duct obstruction, most probably stones, was made.

*Operation.*—(Hunt): June 4, 1938: Transduodenal cautery excision of the ampulla of Vater, with reimplantation of the common duct and the duct of Wirsung into the posterior wall of the duodenum, and T-tube drainage of the common duct. The gall-

bladder was found to be greatly distended and the common duct was dilated to about 1.5 cm. in diameter. Through aspiration of normal colored bile the gallbladder was collapsed and found to contain no stones. Exploratory choledochotomy was unproductive of stones in the common duct, but an olive-tipped probe met obstruction at the ampulla. A tumor, about 1 cm. in diameter, in this area was palpable after the second and third portions of the duodenum had been mobilized. The anterior wall of the duodenum was incised and the tumor involving the ampulla proved to be mobile and not attached to the pancreas. A transduodenal cautery excision of the tumor was made as in Case 1, and, similarly, the severed dilated common duct and duct of Wirsung were reimplanted into the posterior wall of the duodenum. The incision in the duodenum was closed as was the fundus of the gallbladder at the site of its aspiration, and drainage of the common duct was instituted by a T-tube. *Pathologic Diagnosis:* Adenocarcinoma of the ampulla of Vater. Grade III (Fig. 6).

*Postoperative and Subsequent Course.*—Twenty-four hours after operation the temperature was 102° F. pulse 140, following which time improvement continued until the ninth day, when there was some gastric retention, which was controlled within 24 hours by gastric suction drainage. Convalescence continued satisfactorily. Lipiodol injection of the T-tube, on the eighteenth day, showed the material entering the duodenum, and the T-tube was removed. The patient was dismissed from the hospital on the forty-third postoperative day, with the wound healed and general condition good.

The patient remained entirely well until about October 1, 1939, approximately 15 months after the operation, when loss of appetite and weight occurred, with nausea, but no vomiting. Abdominal examination revealed a hard, nodular, tender mass in the upper right quadrant of the abdomen which suggested retroperitoneal metastases. There has been a gradual decline since that time, but on April 1, 1941, 34 months after operation the patient is still living, without recurrent jaundice, but with metastases.

**Case 3.**—St. Vincent's Hospital, No. 2448-40: A woman, age 60, stated, on March 13, 1940, that four months previously painless jaundice had developed and had become progressively more intense. A weight loss of 50 pounds had occurred from a normal weight of 185 pounds. There never had been any biliary colics or other symptoms referable to the biliary tract. The bowels had been constipated, and no gross blood had ever been observed in the stool. Marked edema of the lower extremities had developed during the preceding two months.

Upon examination, emaciation was marked and jaundice was intense. There were areas of excoriation and multiple pustules over the entire body and extremities. The weight was 136 pounds. Blood pressure 118/80. The positive findings on physical examination were: the liver enlarged to the level of the umbilicus; a palpable, distended gallbladder; complete uterine prolapsus; and edema of the lower extremities to the knees (Grade 3).

*Laboratory Data.*—Uranalysis: Specific gravity 1.019, acid reaction, albumin 3+, bile 4, no sugar; microscopic elements absent except for a few pus cells. The concentration of the hemoglobin was 14.4 Gm. per 100 cc. of blood (68 per cent); R.B.C. 3,620,000; W.B.C. 8,000, with a differential count within normal limits; the bleeding time was one minute and the coagulation time was four and one-half minutes; the prothrombin time was not taken until vitamin K and bile salts had been administered for four days, at which time it was 98 per cent of normal (patient 44 seconds, control 42 seconds). The urea content of the blood was 20 mg. No roentgenologic studies were carried out, as a diagnosis of carcinoma of the head of the pancreas or of the terminal common duct seemed justified. After 12 days' hospitalization and preoperative treatment operation was performed.

*Operation.*—(Hunt): March 26, 1940: The Whipple procedure in one stage; resection of second and third portions of the duodenum and the head of the pancreas; ligation and division of the common duct; division and ligation of the duct of Wirsung; cholecystogastrostomy; posterior gastro-enterostomy and choledochostomy; and transfusion



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of 500 cc. of citrated blood during the operation. The distended gallbladder was emptied of 150 cc. of normal colored bile. There were no gallstones. The common duct was found to be dilated to fully 1.5 cm. in diameter and admitted the index finger. A tumor, at least 2 cm. in diameter, was palpated largely within the duodenum, but with some fixation and apparent involvement of the head of the pancreas. Through an incision in the anterior wall of the duodenum, the tumor was accurately visualized and its extent determined (Fig. 7). Even though the tumor invaded the pancreas, it seemed to be an operable lesion, not through transduodenal excision, but through the utilization of Whipple's procedure. The duodenum was divided about 2 cm. distal to the pylorus and the proximal duodenum was inverted. The distal duodenum was divided at approximately the juncture of the third and fourth portions and the distal duodenum was inverted.

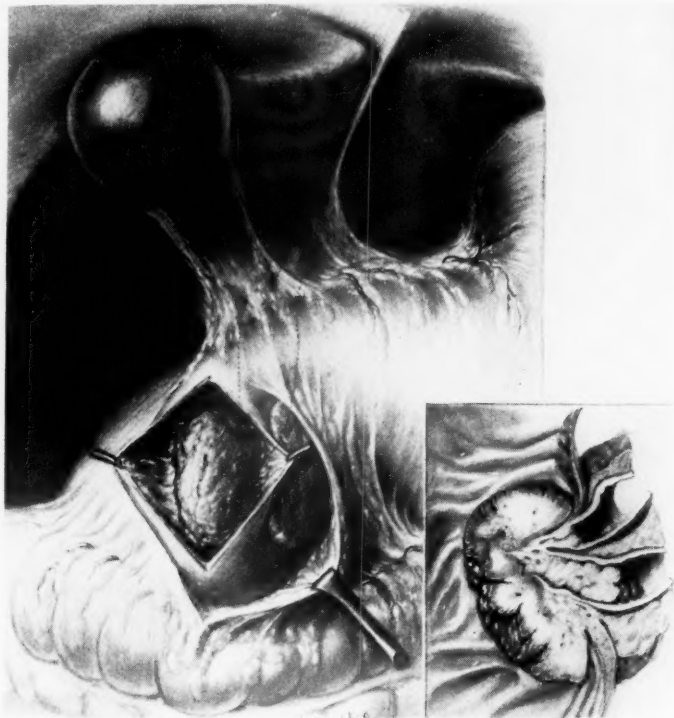


FIG. 7.—Artist's illustration of the tumor in Case 3, visualized upon opening the duodenum. Insert is artist's illustration of sagittal section of tumor.

Approximately three inches of the duodenum containing the tumor were removed *en masse* with part of the head of the pancreas which was resected with the actual cautery, during which procedure the common duct, 1.5 cm. in diameter, and the duct of Wirsung, 8 Mm. in diameter, were divided, with the escape of fully an ounce of pancreatic secretion (Fig. 8). The common duct and the duct of Wirsung were ligated with heavy silk. The severed surface of the pancreatic head was sutured with interrupted sutures of silk and the suture line covered with omentum. A T-tube was placed in the common duct; a cholecystogastrostomy was performed; and the operation completed by a posterior gastro-enterostomy (Fig. 9). Two Penrose drains were inserted to the site of resection. *Pathologic Diagnosis:* Adenocarcinoma, Grade II, of the ampulla of Vater, with invasion of the pancreas (Fig. 12).

*Postoperative and Subsequent Course.*—Considerable shock was manifested, and on the day following the operation a transfusion of 600 cc. of citrated blood was admin-

istered. Progress was entirely satisfactory until the evening of the sixth day, when considerable bleeding occurred from the wound. (It should be stated that suction drainage of the stomach had been instituted immediately after operation and vitamin K had been discontinued.) A prothrombin time determination at the time of bleeding from the wound was 20 per cent of normal (patient 182 seconds, control 38 seconds). Immediate administration of vitamin K and bile salts controlled the hemorrhagic tendency. On the day following the bleeding from the wound, profuse serous drainage oc-

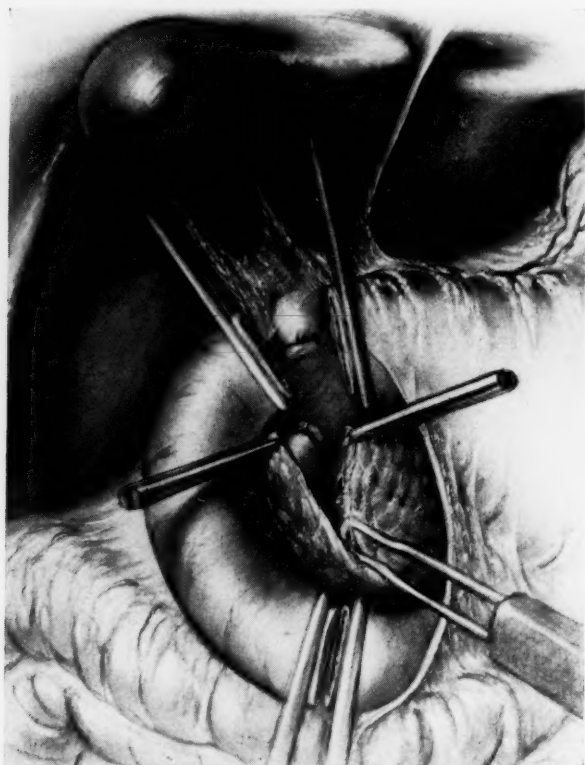


FIG. 8.—Artist's illustration of cautery resection of part of the head of the pancreas and second and third portions of the duodenum, *en bloc*, in Case 3; marked dilatation of the common duct and duct of Wirsung.

curred, which had the characteristics of pancreatic secretion. This drainage continued copiously, and on the eighth postoperative day a catheter was inserted into the wound and through suction applied by the electric pump the wound was kept dry and the amount of secretion, which now contained bile, was measured. Continuous suction was maintained for 19 days, or until the twenty-seventh postoperative day, and the amount of pancreatic secretion and bile from the wound was recorded (Table V). The sinus tract was then firmly packed with gauze, which allowed the wound to heal. The patient was dismissed from the hospital, May 13, 1940, 48 days after operation, with the wound entirely dry. The patient has been seen on a number of occasions, and has continued to make satisfactory progress. She is entirely well, March 26, 1941, one year after operation, with no evidence of recurrence (Fig. 13).

**Case 4.**—St. Vincent's Hospital, No. 479-41: A woman, age 43, was admitted to St. Vincent's Hospital, January 29, 1941. The patient's general health had been good until November, 1940. Thereafter, backache and digestive disturbances characterized by poor

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appetite, nausea and vomiting, and diarrhea without biliary colic comprised the chief complaint until about January 1, 1941, when jaundice developed, which became progressively more intense during the ensuing month. During this time 13 pounds loss of weight occurred.

Upon examination, the patient exhibited some emaciation and moderately deep, generalized icterus. Physical examination was essentially negative. Neither the liver nor gallbladder was palpable. Blood pressure 124/84; weight 103 pounds.

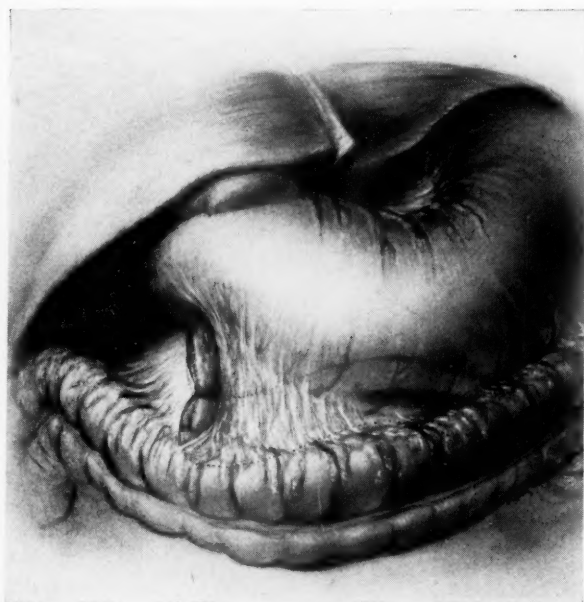


FIG. 9.—Artist's illustration of the operation completed in Case 3. Resection of part of the head of the pancreas and second and third portions of the duodenum *en bloc*, cholecystogastrostomy and posterior gastro-enterostomy all accomplished in one stage.



FIG. 10.—Photograph of the resected duodenum in Case 3 showing the extent of the periampullary involvement of the duodenum.

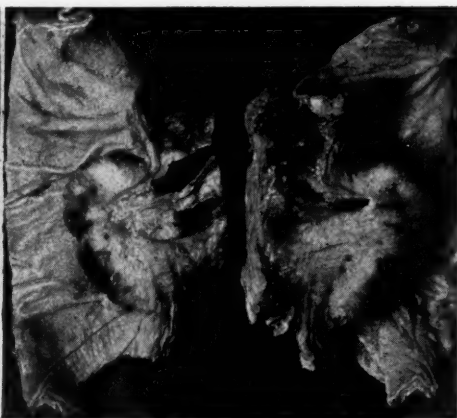


FIG. 11.—Photograph of sagittal section of the resected specimen in Case 3 showing marked dilatation of the common duct and duct of Wirsung; the projection of the tumor into the lumen of the duodenum; and invasion of the head of the pancreas by tumor.

*Laboratory Data.*—Uranalysis gave negative results, with the exception of an occasional pus cell and red cell. The concentration of the hemoglobin was 10.5 Gr. per 100 cc. of blood (63 per cent); R.B.C. 3,280,000; W.B.C. 8,000, with approximately a normal differential count; blood cellular characteristics are here omitted. The prothrombin time was 93 per cent of normal; icteric index 30.2; the benzidine reaction for occult blood in the stool was positive. Gallbladder dye studies disclosed practically no dye in the gallbladder, but, instead, a calcified gallbladder was visualized. Films of the chest, kidneys, ureters, and bladder were negative. Roentgenologic examination of the stomach

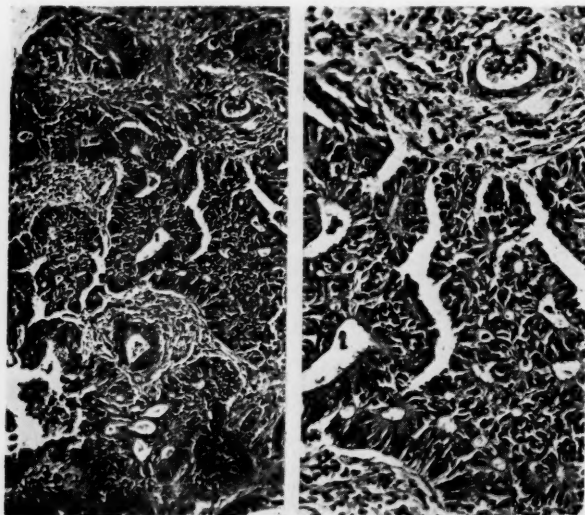


FIG. 12.—Photomicrograph of Case 3: Adenocarcinoma, Grade II (left  $\times 128$ ; right  $\times 245$ ).

and duodenum was negative, except for hyperperistalsis and rapid clearance of the barium from the stomach. Fluoroscopic examination and films of the colon disclosed the absence of the right colon. *Preoperative Diagnosis:* Calculous disease of the gallbladder and common duct.

*First Operation.*—(Hunt): February 1, 1941: Cholecystectomy for calculous disease of the gallbladder and T-tube choledochostomy. Upon opening the abdomen, a thick-walled gallbladder, adherent from a previous protective perforation, was found contracted down on a single large stone. The common duct was greatly dilated. However, exploratory choledochotomy was unproductive of stone in the common or hepatic ducts. An olive-tipped probe passed into duodenum with sufficient difficulty to suggest neoplastic obstruction of the terminal portion of the common duct. The duodenum was mobilized sufficiently for palpation of the second portion of the duodenum and head of the pancreas, in order to provide assurance (which subsequent events proved to be false) that neoplastic disease did not exist. The findings seemed to justify the assumption that pancreatitis existed and was responsible for the obstructive jaundice. T-tube drainage of the common duct was instituted. (Occult blood in the stool was disregarded.)

*Postoperative Course.*—The T-tube was clamped off and the bile was diverted into the duodenum on the twelfth day, and no leakage of bile occurred for nearly a week, when profuse drainage of bile around the tube occurred. A cholangiogram, made on the nineteenth postoperative day, disclosed a complete block at the terminal portion of



FIG. 13.—Photograph of the patient (Case 3), March 26, 1941, one year after operation.

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the common duct. Cholangiographic studies were repeated on the thirty-second day, which again disclosed complete obstruction of the terminal common duct. Occult blood was again found in the stool, which, in spite of the previous findings at operation, justified the diagnosis of a tumor in the periampullary region of the duodenum.

*Second Operation.*—(Hunt): March 5, 1941: Total duodenectomy and cautery excision of part of the head of the pancreas, jejunopancreatostomy; jejunocholedochostomy

FIG. 14.

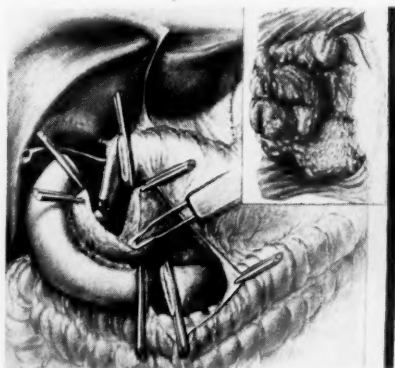


FIG. 15.

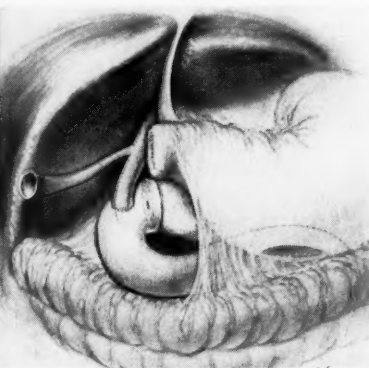


FIG. 14.—Artist's illustration of *en bloc* total duodenectomy and cautery resection of part of the head of the pancreas in Case 4 (cholecystectomy for calculous diseases of the gallbladder and T-tube drainage of the common duct four weeks previously). Insert is artist's illustration of periaampullary involvement of the duodenum.

FIG. 15.—Artist's illustration of operation in Case 4, completed by a long-loop posterior gastro-enterostomy, pancreaticojejunostomy and choledochojejunostomy.

and posterior gastro-enterostomy; T-tube drainage of the common duct was maintained. Upon mobilization of the duodenum, an indurated, somewhat fixed mass in the posterior wall of the duodenum involving the head of the pancreas was encountered which, through an incision in the duodenum, proved to be a periampullary carcinoma. The incision in the duodenum was closed and an extensive resection was carried out. Because of the extensiveness of the induration, only through resection of the entire duodenum from the pylorus to well beyond the ligament or muscle of Treitz with cautery resection of part of the head of the pancreas, could the neoplastic involvement be removed (Fig. 14). A long-loop posterior gastro-enterostomy facilitated drawing the proximal jejunum up through the opening in the transverse mesocolon to suture the open end of jejunum completely over the severed head of the pancreas in a manner to also include and receive the terminal portion of the common duct (Fig. 15). A transfusion of about 600 cc. of citrated blood was administered during the operation. *Pathologic Diagnosis:* Adenocarcinoma of the papilla of Vater, Grade III, with extensive involvement of the duodenum and extension to the head of the pancreas and adjacent lymph nodes (Fig. 18).

*Postoperative Course.*—At no time postoperatively did the temperature exceed 101° F. Drainage of bile around the loosely fitting T-tube was profuse for about five days, after which an electric suction pump facilitated measurement of the drainage which did not exceed 500 cc. in 24 hours. The T-tube was removed from the common duct on the eighth day, and drainage of bile from the wound ceased on the eleventh postoperative day. There was no external loss of pancreatic secretion at any time. The patient was dismissed from the hospital in excellent condition on March 29, 1941, 24 days following the resection.

*DISCUSSION.*—Usually, as carcinoma is encountered in this situation its exact site of origin is entirely indeterminate. Even though these lesions are frequently spoken of as ampullary carcinoma, there is much to support the idea that carcinoma arising within the true ampulla of Vater is extremely



rare. Hanot termed this lesion *cancer du pylore pancratico-billiaire* to distinguish it from those periampullary lesions originating in other structures. Lieber, Stewart, and Lund have recently verified the statements of Rolleston,

FIG. 16.



FIG. 17.

FIG. 16.—Photograph of the mucosal surface of the duodenum in Case 4 showing the extent of the tumor.

FIG. 17.—Photograph of the exterior of the duodenum and resected head of the pancreas with several involved regional lymph nodes; marked dilatation of common duct. Duct of Wirsung entered the common duct proximal to the tumor and was not dilated (Case 4).

Springer, and others, in that, for the most part, these periampullary lesions are primary either in the terminal portion of the common duct, in the pancreatic duct, or in the intestinal mucous membrane overlying the papilla of Vater. As these lesions are encountered upon surgical exploration or at necropsy, all of these structures including the ampulla of Vater usually are involved in the neoplasm, and can be designated only under the broad term, neoplasm of the periampullary region of the duodenum. Practically all malignant lesions occurring in the periampullary region are carcinomata, most frequently adenocarcinoma or papillary carcinoma; although spindle cell sarcoma and melanoma have been reported.

Early metastases are not frequent because, as Cooper has stated, the lesion, by virtue of its strategic position, produces obstructive symptoms early. However, that metastases to the retroperitoneal lymph nodes, liver, lungs, *etc.*, may and do ultimately occur is attested by an incidence of such me-

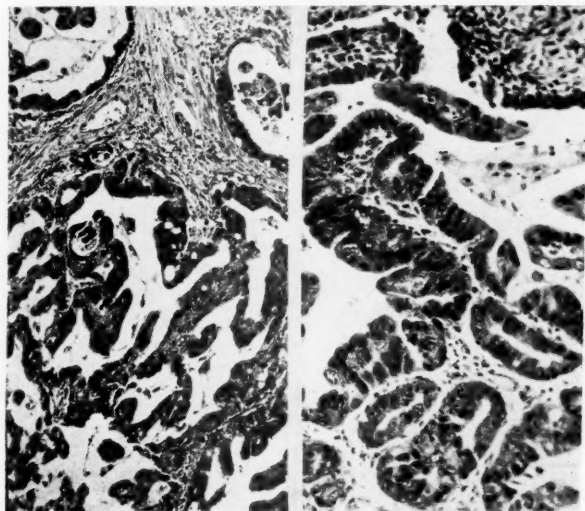


FIG. 18.—Photomicrograph of Case 4: Adenocarcinoma, Grade III (left  $\times 128$ ; right  $\times 245$ ).

tastases in approximately 45 per cent of the cases reviewed by Lieber, Stewart, and Lund, which, for the most part, were the terminal findings at necropsy and not those of surgical exploration early in the course of the disease. Invasion of the pancreas was likewise a terminal finding at necropsy in 20 per cent of the cases.

*Diagnosis.*—The clinical manifestations of periampullary carcinoma are practically always those of obstructive jaundice in which the distended gall-bladder, when palpable, in accordance with Curvoisier's law, leads to the diagnosis of neoplastic obstruction, usually carcinoma of the head of the pancreas. That error in the interpretation of diagnostic criteria may occur, is indicated by Ransom's study of 109 cases of carcinoma of the pancreas and bile ducts, verified by operation or at necropsy, in which the lesion in nine cases was periampullary. The relative frequency with which localized and entirely operable periampullary lesions are found at necropsy in individuals who have not been afforded the opportunity or who have been denied the privilege of surgical exploration through assumed clinical diagnostic accuracy and asserted futility, emphasizes the necessity for surgical exploration in all cases in which the clinical evidence indicates neoplastic obstruction of the terminal portion of the common duct.

Cooper, in 1937, and Lieber, Stewart, and Lund, in 1939, very thoroughly detailed the clinical manifestations of periampullary neoplastic disease. It is worthy of note that lesions in this situation occur in comparative youth. While the average age for 92 out of 124 cases (Table I), where the age was

recorded, was 50.9 years, the age was 35 years or less in eight cases; the youngest individual operated upon was age 17. In many instances pain was an important symptom, frequently of sufficient severity to warrant a diagnosis of calculous obstruction of the common duct, yet seldom was calculous disease of the common duct associated with periampullary neoplastic disease. The presence of occult blood in the stool may seldom be disregarded when obstructive jaundice exists. Denechau *et al.* have suggested that biliary obstruction, intractable diarrhea and intestinal bleeding may give the clue to the diagnosis of ampullary carcinoma. In Cooper's study of 14 cases, occult blood was present in nine of 11 cases in which such investigation was made.

Roentgenologic studies have been of little diagnostic aid in early periampullary disease. Hoffman and Pack reported the roentgenologic findings in 16 cases of carcinoma of the duodenum, seven of which were periampullary lesions. Obstruction in the second portion of the duodenum was demonstrated in one of these, and in two cases there was six-hour gastric retention. Cooper reported the roentgenologic findings in ten cases of periampullary carcinoma. Obstruction at the level of the ampulla was noted in four cases, a filling defect in the duodenum in one case and some flattening of the posterior wall of the duodenum in another case. Positive roentgenologic findings in patients operated upon during recent years were exhibited in cases reported by Brunschwig and Childs, Roscher, and Orr. Cholangiographic studies revealing complete obstruction of the terminal portion of the common duct in conjunction with occult blood in the stool provided the basis for the clinical diagnosis of periampullary carcinoma in Case 4, herein reported.

*Surgical Procedures.*—In 75 per cent of the 124 cases here collected, surgical extirpation of periampullary carcinoma was accomplished by transduodenal excision, and by retroduodenal excision, resection of the duodenum alone, or with a part of the head of the pancreas in the remainder. In 21 cases, transduodenal excision alone was employed with apparently no attempt at restoration of biliary and pancreatic ductal continuity with the duodenum. In the 57 cases, however, in which the common and pancreatic ducts were divided in the course of excision of the tumor, these structures were reimplanted into the posterior wall of the duodenum. In approximately one-half of the cases in which these ductal structures were reimplanted, internal biliary drainage through some anastomotic procedure or external drainage of bile was provided. Internal or external drainage of bile was likewise provided in 15 cases in which the common duct and pancreatic ducts were not reimplanted. This latter procedure and resection of the duodenum with end-to-end anastomosis, and one or another of the various methods of disposing of bile and pancreatic secretion have proved the most hazardous methods of dealing with obstructing lesions in this situation (Table II).

Transduodenal excision, with one or another method of dealing with bile and pancreatic secretion, was actually employed in 85 per cent of the cases until about 1935. Advances which had been made in the surgical extirpation of adenomata of the islet cells of the pancreas and in resection of portions of the pancreas in hyperinsulinism paved the way for Whipple and his asso-

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TABLE II

SURGICAL PROCEDURES IN 124 RADICAL OPERATIONS FOR CARCINOMA OF THE AMPULLA OF VATER  
(1898-1941)

Operation	No. of Cases	Deaths	Per Cent
Transduodenal excision.....	93	27	29.0
Transduodenal excision only.....	21	8	38.0
Transduodenal excision, with reimplantation of common duct or common duct and pancreatic duct.....	30	5	16.6
Transduodenal excision, with reimplantation of common duct or common duct and pancreatic duct with internal or external biliary drainage.....	27	7	25.9
Transduodenal excision, without reimplantation of common duct or pancreatic duct with internal or external biliary drainage.....	15	7	46.6
Retroduodenal excision.....	5	2	40.0
Resection of duodenum, with implantation of common duct or common duct and pancreatic duct and end-to-end anastomosis of duodenum.....	11	5	45.4
Resection of duodenum and head of pancreas.....	15	4	26.6
Total.....	124	38	30.6

ciates to devise and carry out the two-stage operation for periampullary carcinoma, wherein the duodenum and part of the head of the pancreas are resected *en bloc*. Since the presentation of this procedure by Whipple, Parsons, and Mullins, in 1935, approximately 50 per cent of the cases of periampullary carcinoma have been operated upon by their method.

Graham and others have demonstrated that a large part of the pancreas can be excised and that the main pancreatic ducts may be ligated, which has provided an approach to ampullary carcinoma invading the head of the pancreas inoperable to transduodenal methods. Brunschwig, in 1937, carried out, for the first time, this radical two-stage operation for carcinoma of the head of the pancreas. Preservation of external pancreatic secretion is desirable, but the problems of pancreato-intestinal anastomosis are great. Kerr suggested, in 1914, a method of capping the head of the divided pancreas with the distal end of the duodenum. However, the pancreatic capsule does not readily lend itself to such an anastomotic procedure. Tenani, in 1922, Nemenyi, in 1935, and Hunt, in 1941, each accomplished such an anastomosis following resection of the duodenum and head of the pancreas for ampullary carcinoma.

The mortality rate of surgical extirpation of ampullary carcinoma in the 124 collected cases was 30.6 per cent. However, during the past 15 years the mortality rate has been materially reduced. In the 58 cases, collected by Cohen and Colp, the mortality rate was 41.3 per cent, while in 66 cases operated upon since 1925 it was 21.2 per cent (Table III). A trend toward the two-stage operation has developed during the past 15 years, not only as pertains to radical resection of the duodenum and part of the head of the pancreas, but in transduodenal excision as well. Whereas there were eight

TABLE III  
COMPARATIVE MORTALITY RATE, IN 58 CASES (1898-1925); AND 66 CASES (1925-1941)

Operation	1898-1925			1925-1941		
	No. of Cases	Deaths	Per Cent	No. of Cases	Deaths	Per Cent
Transduodenal excision.....	46	20	43.4	47	7	14.9
Transduodenal excision only.....	16	8	50.0	5	0	0
Transduodenal excision, with reim- plantation of common duct or com- mon duct and pancreatic duct....	15	3	20.0	15	2	13.3
Transduodenal excision, with reim- plantation of common duct or com- mon duct and pancreatic duct, with internal or external biliary drainage	8	4	50.0	19	3	15.8
Transduodenal excision, without reimplantation of common duct or pancreatic duct, with internal or external biliary drainage.....	7	5	71.0	8	2	25.0
Retroduodenal excision.....	4	2	50.0	1	0	0
Resection of duodenum, with implan- tation of common duct or common duct and pancreatic duct and end-to- end anastomosis of duodenum.....	8	2	25.0	3	3	100.0
Resection of duodenum and head of pancreas.....	0	—	—	15	4	26.6
Total.....	58	24	41.3	66	14	21.2

two-stage operations in the first 58 cases, collected by Cohen and Colp, there were 20 two-stage operations in 66 cases, collected since 1925, with a mortality rate of 25 per cent as compared to 19.5 per cent in 46 one-stage operations.

In the past, operative and postoperative bleeding has been the chief hazard of the surgical procedures for extirpation of ampullary carcinoma. Hemorrhage accounted for 31 per cent of the deaths, when the cause of death was stated (Table IV). However, it is more than probable that the cause of

TABLE IV  
CAUSE OF DEATH IN 38 CASES (1898-1941)

Cause	No. of Cases	Per Cent
Hemorrhage.....	12	31.5
Peritonitis.....	5	13.1
Duodenal fistula.....	3	7.8
Shock.....	2	5.2
Pneumonia.....	2	5.2
Not stated.....	14	36.8

death was hemorrhage in fully 50 per cent of the cases, had the cause of death been stated in each instance. Peritonitis, duodenal and pancreatic fistula, shock and pneumonia likewise have been rather prominent and important causes of death. Among the postoperative complications, duodenal and pancreatic fistulae materially prolong convalescence and provide many problems in their management.



# PERIAMPULLARY CARCINOMA

*Pancreatic Fistula.*—The amount of secretion which may be lost through the wound once a pancreatic fistula develops is at times surprisingly large, particularly when the secretion consists of all the pancreatic secretion and bile. Snyder and Lium, who intubated the duct of Wirsung following transduodenal excision of a carcinoma of the ampulla, collected the pancreatic secretion for 12 days. There was great variation in the amount of pancreatic secretion each 24 hours, as influenced by many factors. However, during the last four days in which drainage was maintained, the average daily output

TABLE V  
DAILY 24-HOUR OUTPUT OF PANCREATIC SECRETION AND BILE  
(CASE 4) BY SUCTION DRAINAGE

1940	Amount Cc.
April 4 From 9:30 A.M.....	1,350
April 5.....	1,030
April 6.....	1,800
April 7.....	1,975
April 8.....	1,680
April 9.....	1,550
April 10.....	1,680
April 11.....	1,575
April 12.....	1,250
April 13.....	750
April 14.....	1,500
April 15.....	1,470
April 16.....	1,600
April 17.....	1,180
April 18.....	1,200
April 19.....	1,130
April 20.....	920
April 21.....	1,200
April 22.....	940
April 23 7:00 A.M. to 10:50 A.M.....	175
April 27 From 10:50 A.M.....	1,100
April 28 7:00 A.M. to 11:45 A.M.....	350

of pancreatic secretion was 1,167 cc., with a maximum of 1,384 cc. Bile-tinged secretion amounting to as much as 1,500 cc. in 24 hours in Ransom's case practically ceased by the eighteenth postoperative day. In my own Case 3, the measured daily output of secretion consisting of bile and pancreatic secretion averaged 1,356 cc. for 19 days, with a maximum 24-hour output of 1,975 cc. (Table V). A tendency exists for a pancreatic fistula to cease draining spontaneously if and when communication with the intestinal tract occurs. Such spontaneous closure apparently occurred in the cases of Ransom, Hunt, and Hollenberg, even though eight to nine months elapsed in the latter case. A pancreatic fistula persisted in Orr's case at seven months, and after three months in Orator's case. In the latter instance, external diversion of secretion from the fistula to a jejunostomy was accomplished.

*Results of Operation.*—In general, the results of surgical extirpation of ampullary carcinoma have not been good (Table VI). The follow-up is entirely inadequate, and the ultimate result in those surviving the operation is not known, except as it was, for the most part, obtained from the original case report. The information available to me disclosed that 41 per cent of

TABLE VI

RESULTS IN 86 CASES WHICH SURVIVED RADICAL REMOVAL OF CARCINOMA  
OF THE AMPULLA OF VATER AND PERIAMPULLARY PORTION OF THE DUODENUM

Subsequent course not recorded.....	15
Reported living and well.....	36
1- 6 months.....	8
6-12 months.....	11
12-18 months.....	5
2 years.....	2
3 years.....	4
4 years*.....	3
5 years.....	1
8 years.....	1
9 years.....	1
Living with pancreatic fistula.....	2
3 months and 7 months	
Living with metastases.....	2
23 months and 3 years	
Death from recurrence or metastases.....	26
Within 6 months.....	10
6-12 months.....	6
12-18 months.....	1
18-24 months.....	3
24-30 months.....	4
30-36 months.....	1
56 months.....	1
Death from other causes, without evidence of recurrence or metastases	5
8-12 months.....	3
2 years.....	1
3 years.....	1

\* One of these (Koerte's Case 2) was reported by Muller and Rodemaker, also by Whipple, Parsons, and Mullins to have survived 22 years.

the patients surviving the operation were living and well up to nine years. One of these, Koerte's Case 2 (Table I), operated upon in 1905, was reported by Muller and Rodemaker, and also by Whipple, Parsons, and Mullins to have survived for 22 years. Two other cases (Van Ardenne and Van Remyne) which were not available to me, were reported by Muller and Rodemaker living five and six years, respectively. It would appear that perhaps 12 persons, or approximately 14 per cent, of those who survived the operation were living and well for periods varying from three to 22 years. That one may live for some time, even with recurrence and metastases, is proved by the case reported by Muller and Rodemaker, in which the patient survived four years and eight months after operation. Death from recurrence or metastases occurred in 30 per cent of the cases within one year or thereabouts, but several patients lived for from two and one-half to three years.

That radical surgical procedures are warranted early in periampullary carcinoma, is emphasized by the statistical review of Lieber, Stewart, and Lund. Ninety-seven of 100 patients who were not operated upon lived from two weeks to 28 months, an average of 6.6 months. Sixty-one, or two-thirds of these, died within six months, while 90 per cent lived less than one year, and interestingly enough, four lived for from 22 to 28 months. Palliative operation was performed for the relief of jaundice, with a mortality rate of 76.4 per cent within the first 19 days; nine survived from one to 60 months,

an average of 19 months, and three were living at the end of four, four and one-half, and 42 months, respectively. Certainly, the mortality rate of radical operation throughout the entire period since Halsted's first radical operation, has been materially less than that for palliative operations. Judd and Hoerner have stated that patients who survive resection or excision live longer than those in whom simple palliative operations are performed.

Even though part of the head of the pancreas was included in the resection of the duodenum for periampullary carcinoma by Kausch, in 1909, Hirschel, in 1913, Tenani, in 1922 and Denks, in 1929, the radical operation of Whipple, Parsons, and Mullins provides a method for resection wide of the lesion, through which hope may be engendered for improvement in the ultimate results of surgical extirpation of periampullary neoplastic disease.

#### SUMMARY

Four cases are reported in which carcinoma of the periampullary portion of the duodenum was successfully removed. Transduodenal resection of the ampulla of Vater and terminal portion of the common and pancreatic ducts, with reimplantation of these ducts into the posterior wall of the duodenum comprised the surgical procedure in two cases; the various procedures facilitating resection of the duodenum and head of the pancreas by the method of Whipple, Parsons, and Mullins in two stages was successfully carried out in one-stage in one case; in the fourth case, cholecystectomy for calculous disease of the gallbladder and T-tube drainage of the common duct preceded the second-stage operation of total duodenectomy, resection of the head of the pancreas, pancreaticojejunostomy, choledochojejunostomy and posterior gastro-enterostomy.

A collective review of 124 cases of radical operation for ampullary carcinoma is presented, which provides the basis for an analysis of the various surgical procedures, their mortality rate, and the results, in general, of radical extirpation of neoplastic disease in this situation.

Abstracts of 32 cases, not previously collected, are appended:

#### ABSTRACTS OF 32 CASE REPORTS OF RADICAL OPERATION FOR CARCINOMA OF THE AMPULLA OF VATER, COLLECTED SINCE 1935\*

\*The first 11 of these were operated upon previous to 1935, but were not included in the collective reviews of Cohen and Colp, in 1927; Hunt and Budd, in 1935; or by Whipple, Parsons, and Mullins, in 1935.

**BÖHM** (reported by Kerr): The patient, a man, age 52, six weeks previous to admission, developed jaundice not accompanied by pain, loss of appetite, weight or strength. A diagnosis was made of tumor of the head of the pancreas or the ampulla of Vater. At operation, May, 1910, transduodenal excision of a hazelnut-sized tumor of the ampulla was made and the common duct and the duct of Wirsung were reimplanted into the posterior wall of the duodenum. The pathologic report was adenocarcinoma.

*Subsequent Course:* Two years after operation the jaundice recurred and a posterior gastro-enterostomy was performed for local recurrence. The patient lived nearly one year thereafter.

**SCHÜSSLER** (two cases): Case 1.—The patient, a man, age 43, had had painless jaundice for three months. At operation, a tumor at the ampulla of Vater was found. A resection of the duodenum was performed and the common duct and duct of Wirsung were reimplanted into the duodenum. The patient died of hemorrhage on the ninth day. The pathologic report was carcinoma of the ampulla of Vater.

Case 2.—A woman, age 34, had had severe biliary colic and jaundice of five weeks' duration. At operation, July 12, 1919, a transduodenal excision of the tumor of the ampulla was made and the common duct was reimplanted into the duodenum. A posterior gastroenterostomy was added. The patient was reported to be in good health at the end of four months. The pathologic report was carcinoma of the ampulla of Vater.

BLAD: The patient, a woman, age 62, had for eight months gradually progressive jaundice and hemorrhage from the nose and from the intestinal tract. At operation, February 24, 1920, a tumor about the size of an olive was palpated at the terminal portion of the common duct. A transduodenal excision of this tumor was made with reimplantation of the common duct into the duodenum; 16 months after operation the patient was in good health. The pathologic report was adenocarcinoma of the ampulla of Vater.

BRENNER (reported by Eppinger and Walzel): The patient was a man, age 58, who had had occasional gallbladder colics for nine years. Previous to admission, there had been upper right quadrant pain, followed by jaundice. At operation in November, 1924, a tumor was palpated in the second portion of the duodenum. The duodenum was incised and the tumor of the posterior wall of the duodenum was excised. The case is reported by Eppinger and Walzel as one of neoplastic obstruction of the terminal portion of the common duct.

EISELSBERG (reported by Eppinger and Walzel) (two cases): Eppinger and Walzel report two cases of carcinoma of the ampulla of Vater which were removed by transduodenal excision. No statement is made of the disposition of the common duct or the duct of Wirsung. Recovery occurred in one of these patients and the other patient died on the third day of hemorrhage.

LAGOS, UGÓN, AND DOMINGUEZ: The patient, a man, age 41, had painless, progressive jaundice of three months' duration. A diagnosis was made of probable neoplasm of the head of the pancreas. At operation in April, 1926, a transduodenal excision of a small tumor at the ampulla of Vater, a little less than 1 cm. in diameter, was accomplished. The common duct was reimplanted into the posterior wall of the duodenum. Death occurred 16 hours later from hemorrhage. The pathologic report was carcinoma of the ampulla of Vater.

DE BEULE (three cases): The author operated upon three cases of carcinoma of the ampulla of Vater. In each of two patients the tumor, the size of a hazelnut, was removed by transduodenal excision with reimplantation of the common duct into the posterior wall of the duodenum. In one of these patients, massive metastases to the liver occurred within a few months after operation. The other patient survived for three years and died of influenza. The tumor in the third patient, the size of a pigeon's egg, was ulcerating, and was removed by resection of the duodenum with end-to-end anastomosis, following which a cholecystogastrostomy was performed. This patient died following the operation.

SNYDER AND LIUM: The patient, a man, age 48, was admitted to the hospital, March 31, 1934, with a history of jaundice of 12 weeks' duration, and a loss of weight of 35 pounds. At operation, a firm tumor, about 1.5 cm. in diameter, at the ampulla of Vater was palpated. Cholecystoduodenostomy was performed, and the common duct was drained. Five weeks later, a transduodenal excision of the tumor of the ampulla of Vater was performed. A catheter was inserted into the dilated duct of Wirsung after the duct had been reimplanted into the posterior wall of the duodenum, and the catheter was brought out through the duodenum and anterior abdominal wall. Catheter drainage of the duct of Wirsung was maintained for 11 days. During the last four days of this period the average daily output of pancreatic secretion amounted to 1,167 cc. A subsequent local recurrence necessitated another surgical procedure, with recovery. Pathologic studies proved the tumor to be carcinoma, probably originating in the common duct.

KAFKA: A man, age 52, had progressive, painless jaundice for about four months. At operation, October 9, 1935, transduodenal excision of a bean-sized tumor at the ampulla was accomplished, and the common duct and the duct of Wirsung were reimplanted into the posterior wall of the duodenum. Twenty months after the operation the patient was entirely well, but two years after the operation death occurred from unknown cause. The pathologic report was carcinoma.

NEMENYI: The patient, a man, age 42, had had progressive, painless jaundice for three months with a loss of weight of 40 pounds. At operation, December 12, 1935, a tumor was palpated at the ampulla of Vater. The duodenum containing the tumor and a small section of the pancreas were resected. The pancreatic duct was not seen, but the common duct traversed the pancreas remaining. The distal, open end of the duodenum was sutured over the head of the pancreas. A loop of jejunum was anastomosed to the proximal duodenum and an entero-anastomosis was made between the two limbs of the jejunum. Sixteen months after the operation the patient was entirely well, having regained nearly all his weight. The pathologic report was adenocarcinoma of the ampulla of Vater.

BUMM (reported by Geisthövel): A man, age 54, had had digestive disturbance for about two years, without biliary colic, and had been jaundiced for about 18 months. There had been occasional chills and fever, and the patient had lost 30 pounds in weight. At operation, in February, 1936, a cherry-stone-sized tumor at the ampulla of Vater was exposed through an incision in the duodenum. A transduodenal excision of the tumor was accomplished, and the common duct and the duct of Wirsung were reimplanted into the posterior wall of the duodenum. A cholecystoduodenostomy was made at the site where the duodenum had been opened. Six months after operation the patient had gained 22 pounds, and was well. The pathologic report was carcinoma of the ampulla of Vater.

**ORATOR:** A woman, age 48, had had epigastric discomfort for two months, loss of appetite, and only slight jaundice. Roentgenologic examination disclosed an obstructing lesion of the duodenum. At operation, January 25, 1936, a hen's egg-sized tumor of the duodenum attached to the head of the pancreas was found. A posterior gastro-enterostomy and cholecystogastrostomy comprised the first-stage operation. On February 6, 1936, 12 days later, the second stage resection of the duodenum and head of the pancreas, was performed, after the method of Whipple, Parsons and Mullins. A pancreatic fistula developed shortly after operation and the daily loss of pancreatic secretion varied between 300 and 500 cc., which by the end of about four weeks decreased to 200 cc. With a pancreatic fistula persisting a high jejunostomy was performed, so that the pancreatic secretion from the fistula could be injected into the jejunum. The subsequent course is not reported. The pathologic report was annular adenocarcinoma of the duodenum with invasion of the pancreas.

**HYDE AND YOUNG:** A woman, age 76, was admitted to Faulkner Hospital, October 26, 1936, on account of jaundice for two weeks. Blood in stool by guaiac test ++ on one of two occasions. *Preoperative Diagnosis:* Carcinoma of the pancreas. At operation, November 17, 1936, transduodenal excision of a tumor of the ampulla of Vater, 1.5 by 1 by 0.6 cm. in diameter, with reimplantation of the common duct and the duct of Wirsung into the posterior wall of the duodenum was accomplished. The common duct was drained externally. Annual follow-up studies have revealed an apparent cure after three years. The pathologic report was adenocarcinoma of the ampulla of Vater.

**HOLLENBERG** (personal communication from Whipple): The patient, a woman, age 45, was mildly jaundiced and had lost 30 pounds in weight. There was blood in the stool. In March, 1936, the first-stage of the Whipple operation was performed, and one month later a resection of the duodenum and part of the head of the pancreas was accomplished for a carcinoma of the ampulla of Vater, about 3 cm. in diameter. A nonirritating pancreatic fistula developed which persisted for eight to nine months. Following lipiodol injection of the sinus, which disclosed communication with the small intestine, the drainage ceased spontaneously. Thereafter excellent health was experienced for a year and a half. Clinical manifestations of local recurrence developed without jaundice and death occurred in February, 1939, slightly less than three years after the resection.

**HOFFMAN AND PACK:** A man, age 58, had recurrent jaundice, chills and fever. A diagnosis was made of an impacted stone in the common duct. At operation, by Doctor Pickhardt, the common duct was found to be obstructed at the ampulla, but no stone was found, and the common duct was drained by a T-tube. At the end of four weeks a copious hemorrhage occurred from the gastro-intestinal tract and from the wound. Following transfusion, a tumor involving the ampulla of Vater which was excised. Death occurred six hours later. The pathologic report was adenocarcinoma.

**MALLET-GUY:** A woman, age 56, had had repeated biliary colic, chills, fever and jaundice; had been operated upon several times and stones had been recovered from the common duct. At operation, April 8, 1938, a transduodenal excision of a small tumor obstructing the ampulla of Vater was performed, and the common duct was drained externally. Recovery occurred. The pathologic report was epithelioma(?).

**MCCABE:** The patient, a man, age 67, had had painless jaundice for three months, during which time the weight loss was 30 pounds. Epigastric pain, vomiting and diarrhea were manifested during the three weeks preceding admission. At operation, July 16, 1937, a tumor the size of a hen's egg, mobile and soft in consistency, was palpated in the second portion of the duodenum and transduodenal excision of the tumor was performed. The common duct and the duct of Wirsung were reimplanted into the posterior wall of the duodenum. The common duct was drained by a T-tube. Bleeding from the wound, stomach, bowel and kidneys occurred on the fifth postoperative day and continued for a week, finally subsiding following daily transfusion. The convalescence thenceforth was entirely satisfactory. The pathologic report was adenocarcinoma.

**BRUNSCHWIG AND CHILDS:** The patient, a woman, age 41, was admitted, October 22, 1937, chiefly because of increasing fatigue, an increase in the quantity of stool and irregular periods of frequent stools. The stools had been foul and varied in color from clay-colored to dark brown. There was no history of jaundice. Upon examination, a vague, deep mass the size of an egg was palpable to the right and slightly above the umbilicus. The stools contained occult blood. Roentgenographic examination disclosed a tumor mass, approximately 8 by 5 cm., within the distended second portion of the duodenum. The preoperative clinical diagnosis was a neoplasm of the pancreas or duodenum with partial obstruction of the pancreatic ducts. At operation, November 26, 1937, a one-stage transduodenal excision of the tumor was performed, with reimplantation of the common duct and the duct of Wirsung into the posterior wall of the duodenum. At the end of 15 months, the weight had been regained and there was much improvement in the patient's general condition. The pathologic report was carcinoma (possibly carcinoid) of the second portion of the duodenum with involvement of the ampulla of Vater.

**ROSCHER:** The patient, a man, age 55, had loss of appetite and weight and progressive obstructive jaundice for four to five months. Roentgenologic examination of the stomach and duodenum disclosed what was interpreted as an ulcerating tumor in the region of the papilla of Vater. At operation, in March, 1936, a cholecystogastrostomy was performed. Two months later the second-stage resection of the duodenum and part of the head of the pancreas, division and ligation of the common duct, implantation of the duct of Wirsung into the jejunum and posterior gastro-enterostomy



were performed. Death occurred five months after operation of bronchopneumonia. The pathologic report was carcinoma of the papilla of Vater.

**DIVIS** (reported by Kafka, 1937): The patient was a woman, age 65, who had an obstructive jaundice. April 30, 1937, stones were removed from the gallbladder and one-stage transduodenal excision of tumor, with reimplantation of the common duct and duct of Wirsung into duodenum and cholecystoduodenostomy were accomplished. Death occurred one year after the operation from a cardiac lesion.

**TROUT**: The patient, a man, between 55 and 60 years of age, was operated upon for a carcinoma of the ampulla of Vater, with invasion of the head of the pancreas. The operation consisted of cholecystojejunostomy, posterior gastro-enterostomy, division and ligation of the common duct just below the cystic duct, resection of the duodenum and head of the pancreas *en bloc* in one stage. Death occurred within a few hours after the operation.

**RIVER, McNEALY AND RAGINA** (three case reports): Case 1.—(McNealy): A woman, age 63, was admitted to the Cook County Hospital, December 12, 1937, with the complaint of dull, boring epigastric pain and progressive jaundice of four weeks' duration. The stools contained occult blood on several occasions. A diagnosis of obstructive jaundice, probably due to a malignant lesion, was made. At operation, January 8, 1938, transduodenal resection of a tumor of the ampulla of Vater was made and the common duct and duct of Wirsung were reimplanted into the posterior wall of the duodenum. Approximately 16 months later jaundice, chills and fever recurred. At operation, August 23, 1939, cicatricial stenosis at the site of the reimplantation of the common duct into the posterior wall of the duodenum was found. A cholecystogastrostomy was performed. The patient was well two years and two months following excision of the tumor. The pathologic report was adenocarcinoma of the ampulla of Vater with invasion of the common duct and the pancreatic duct.

Case 2.—(River): The patient, a man, age 55, was admitted to the Cook County Hospital, July 4, 1939, because of jaundice of eight months' duration, loss of 58 pounds in weight, and pain in the upper right quadrant of the abdomen. At operation, July 20, 1939, the common duct and the gallbladder were drained. Jaundice recurred at the end of three weeks immediately following closure of the biliary fistula. The persistence of blood in the stool suggested the diagnosis of carcinoma of the ampulla of Vater. Operation, August 15, 1939, consisted of transduodenal excision of the ampullary tumor with reimplantation of the common duct into the posterior wall of the duodenum. Eight months later, jaundice, chills and fever suggested cicatricial stenosis of the common duct. A cholecystojejunostomy, after the method of Whipple, was followed by recovery. The pathologic report was adenocarcinoma of the terminal portion of the common duct.

Case 3.—(River): The patient, a man, age 55 years, was admitted to the Cook County Hospital, September 6, 1939, on account of jaundice of four weeks' duration, pain in the upper right quadrant of the abdomen and weight loss of ten pounds. At operation, September 29, 1939, transduodenal excision of a tumor, 1.3 cm. in diameter, at the ampulla of Vater was made and the common duct and the duct of Wirsung were reimplanted into the posterior wall of the duodenum. External drainage of the biliary tract was provided by cholecystostomy. The patient was entirely well nine months later. The pathologic report was papillary adenocarcinoma of the pancreatic duct.

**MADDOCK**: A man, age 36, was admitted to the University of Michigan Hospital, January 13, 1940, on account of jaundice and intermittent diarrhea of three months' duration. The patient had had severe stabbing pain in the upper right quadrant of the abdomen. At operation, January 22, 1940, an incision in the duodenum exposed a tumor of the ampulla of Vater. A resection of the second portion of the duodenum including the tumor was accomplished, with end-to-end anastomosis restoration of the duodenum. The common duct was implanted into the first portion of the duodenum and the gallbladder was removed. Death occurred on the fourteenth day from peritonitis. The pathologic report was adenocarcinoma of the ampulla of Vater.

**ORR**: The patient, a man, age 47, was admitted to the University of Kansas Hospital, April 24, 1940, on account of painless, progressive jaundice and weight loss of 30 pounds during the preceding four months. Operation.—First stage: Upon surgical exploration April 30, 1940, a firm mass, 1 cm. in diameter, was palpated at the ampulla. An anastomosis between the common duct (gallbladder absent) and the stomach was made and a posterior gastro-enterostomy completed the first-stage operation. Second-stage operation.—May 15, 1940: The terminal common duct was ligated and divided, the duodenum from the pylorus, to well below its second portion, and a wedge-shaped section of the head of the pancreas were resected. The pylorus and distal duodenum were closed and the defect in the pancreas was closed with interrupted sutures of silk. Following the operation there was profuse drainage of clear fluid from the wound. The patient was readmitted to the hospital several times subsequently on account of persistence of the pancreatic fistula. Seven months after operation the patient had regained the 25-pound weight loss. Moderate drainage from the pancreatic fistula persisted. The pathologic report was adenocarcinoma of the ampulla of Vater.

**RANSOM**: J. K., a man, was admitted to the University of Michigan Hospital, December 14, 1940, on account of painless, progressive jaundice of one month's duration, and a weight loss of 12 pounds. *Clinical Diagnosis*: Obstructive jaundice probably due to carcinoma of the head of the pancreas. Operation.—December 24, 1940: A movable, olive-sized tumor was found at the ampulla of Vater. The first-stage of the Brunschwig operation was carried out, which consisted of a posterior gastro-enterostomy, cholecystojejunostomy and entero-anastomosis between the two limbs of jejunum. At the second operation, January 21, 1941, the resection included the first and second portions of

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the duodenum and the head of the pancreas. The pyloric end of the stomach and distal duodenum were closed, the pancreatic duct and the common duct were ligated, and the end of the pancreas was closed with mattress sutures. On the fourth day after operation, a moderate amount of clear fluid drained from the wound, which two days later became bile-tinged. At one time the fistulous tract drained as much as 1,500 cc. in 24 hours. By the eighteenth postoperative day drainage from the wound had practically ceased. Twenty-five days after the resection the patient was still in the hospital, but was progressing satisfactorily.

**WHIPPLE:** The patient, a man, age 58, was operated upon in October, 1939, for carcinoma of the ampulla of Vater, in whom the radical two-stage operation was performed, with excision of the duodenum and part of the head of the pancreas. This patient is well, has regained his weight, is free from jaundice, and has no digestive disturbance, 15 months after operation.

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DISCUSSION.—DR. MORRIS K. SMITH (New York, N. Y.): I have recently had an experience with a case which corresponded in many ways to Doctor Hunt's last patient. As the matter of diagnosis is almost as difficult as the treatment, it seems worth while to emphasize the point Doctor Hunt made of the significance of blood in the stool.

In my patient I performed a cholecystectomy and drainage of the common duct, but failed to feel a tumor in the duodenum. After two weeks, the stools continuing clay-colored and bile drainage as profusely as ever, a cholangiogram was made which showed a smooth contour of the dilated duct with complete block at the duodenal end. The patient, who had been carefully studied in hospital prior to operation, had shown one unexplained and persistent finding—*occult blood in the stool*. This combination of bleeding and obstruction at the terminus of the common duct, as in Doctor Hunt's case, pointed the way to the diagnosis.

In my patient, we made one further test, duodenal intubation, and obtained contents which were grossly bloody. At the second operation a periampullary carcinoma of the duodenum, resembling grossly the ordinary carcinoma of the large bowel, was found.

DR. THOMAS E. JONES (Cleveland): Many of these cases are deeply jaundiced when they come in for surgery. At operation, we do not know about the patency of the cystic duct. If cholecystogastrostomy is performed, very often there may be a kinking near the duct, and many of these cases will die before they reach the second stage, because we do not get good biliary drainage.

To obviate this difficulty, in the successful case which I had I put a T-tube in the common duct. This gives good drainage immediately, and at the second-stage the patient is in very much better condition. In the first-stage I used a T-tube drainage of the common duct and established a gastro-enterostomy. In the second-stage we removed the head of the pancreas and anastomosed the common duct to the jejunum. The case developed a pancreatic fistula, but he was able to leave the hospital in 36 days. This was about four months ago, so the end-result is not known.

DR. DALLAS B. PHEMISTER (Chicago): There have been three cases operated upon in our clinic—16 months, two and a third years, and three years ago—by the technic described by Doctor Hunt for his first case, which have remained well. In two cases an additional cholecystogastrostomy was performed for fear there might be subsequent stenosis of the common duct. I do not know that it made any difference.

The question of roentgenologic diagnosis was referred to. In one of these patients the roentgenologist did not locate the lesion, but we did not send the patient in with the presumptive diagnosis of carcinoma of the ampulla. In one case, the patient entered with a cholecystotomy sinus, and we injected lipiodol through the fistula. The gallbladder and bile ducts filled, and obstruction was shown at the outlet of the common duct. The patient was reexamined, a barium meal being given first, which showed a defect in the region of the ampulla. Then the gallbladder and bile duct were injected. Both methods of examination confirmed the diagnosis of carcinoma of the ampulla. I think that if such patients are sent to the roentgenologist with the tentative diagnosis of ampullary pathology they will more frequently recognize the lesion.

DR. THOMAS G. ORR (Kansas City, Kans.): Following palliative operation a patient with proven carcinoma of the ampulla has been known to live 33 months; after transduodenal resection patients have lived 4 to 22 years; and after resection of the duodenum and head of the pancreas one patient has lived 34 months, although the average length of life in each of these groups is much shorter. The average time of survival of patients with carcinoma of the ampullary region is shown in Table I. The results of the radical operation, as shown in this table, justify the procedure, without question.

The mortality of the palliative operation has been recorded by Collier and Winfield as low as 26+ per cent, and by Lieber, Stewart and Lund as high as 78+ per cent.

TABLE I

## AVERAGE LENGTH OF LIFE

Without treatment (Outerbridge).....	7.3 mos.
With palliative operation (Judd and Parker).....	7.7 mos.
With radium and roentgen-ray treatment (Pack and McNeer).....	8.0 mos.
With radical operation (Hunt's review) 30 cases dead.....	1.7+ yrs.
With radical operation (Hunt's review) 34 cases still living last report....	2.5+ yrs.

The average mortality of the radical operation in the cases collected by Hunt was 30+ per cent. With present methods of controlling the bleeding tendency in jaundice and treating liver damage, the operative mortality of excision of ampullary tumors should soon compare favorably with operations upon the stomach and rectum for carcinoma.

The choice of the transduodenal or Whipple operation should depend upon the extent of the lesion found at operation. With the recorded excellent results of the former technic we must assume that the more radical procedure is not necessary when the tumor is small and confined to the ampulla. However, the Whipple technic more nearly fulfills the requirements of an operation for carcinoma, in that the region of early extension of the tumor is removed. Carcinoma arising in the pancreas and involving the common duct or ampulla is suitable only for the Whipple operation.

The percentage of carcinomata involving the ampulla or ampullary region which are suitable for radical excision is not yet known. The total number of these tumors as compared to carcinomata in the remainder of the pancreas is also not known. In a recent study of 52 cases of proven carcinoma of the pancreas and ampullary region, 17 or 32 per cent were found in the latter group (Schnedorf and Orr). This is a small number but probably indicates the approximate percentage of tumors arising in the ampulla as compared to tumors having their origin in the pancreas.

The remote effect of excision of a portion or all of the head of the pancreas without reimplantation of the pancreatic duct into the intestine has not yet been studied. Experimental work by Dragstedt indicates that sclerosis of the pancreas may result, followed by fatty infiltration of the liver due to the loss of the hormone lipocin. A careful study of necropsy material will decide this point in the future.

In order to obtain relatively accurate statistical records of patients operated upon, supplementary reports must be made indicating the length of life after operation. In the series reviewed by Doctor Hunt, more than one-third of the cases have no recorded final report.

Below is a follow-up report of one case and a brief record of a new case. Both of these patients were operated upon by the Whipple technic.

**Case 1.**—My first case which was reported at a meeting of the Western Surgical Association in December, 1940, is still alive 11½ mos. after the second stage of the operation. On April 6, 1941, he was operated upon for complete obstruction of the ileum due to a band of adhesions. He still has a small fistula from his jejunum which intermittently opens and discharges for a few days. There is no evidence of pancreatic fistula.

**Case 2.**—M. C. B., female, age 67, was admitted to the University of Kansas Hospital, November 16, 1940. The history and findings were those of carcinoma of the ampulla. A cholecystogastrostomy and gastro-enterostomy were performed November 23, 1940. A very stormy convalescence followed, and after 49 days she was sent home to recuperate.

This patient was readmitted to the Hospital, March 10, 1941, and the second stage of the Whipple operation was performed, March 24, 1941. The duodenum and entire head of the pancreas were resected. The pathologist's report of the tumor removed was "ulcerating adenocarcinoma of the ampulla of Vater with extension into the head of the pancreas and regional lymph nodes."

An uncomplicated postoperative recovery was made and the wound was completely healed within 16 days.



**FIFTY-TWO PROVEN CASES OF CARCINOMA OF THE PANCREAS  
AND THE AMPULLA OF VATER: WITH SPECIAL REFERENCE  
TO FATTY INFILTRATION OF THE LIVER**

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CANCER OF THE PANCREAS constitutes about 1 to 2 per cent of all malignancies. Ewing<sup>1</sup> states that it was found in 1.76 per cent of Kaufmann's autopsies on malignant tumors, and in 2 per cent of Korte's autopsies on 2,943 cases of cancer. He states that Bashford collected 1,000 cases of carcinoma of the pancreas in 84,000 cancers.

The analysis of 40 autopsies by D'Aunoy, Odgen and Halpert<sup>2</sup> indicates a grave prognosis and rapidly fatal outcome of the disease. In 38 of the 40 patients, the clinical course of the illness lasted one to eight months, with an average duration of four and one-half months. A similar hopeless outlook is expressed by Lahey and MacKinnon<sup>3</sup> in their analysis of 47 cases, and by Kauer and Glenn<sup>4</sup> in their study of 32 cases.

In 1935, Whipple, Parsons, and Mullins<sup>5</sup> reported the successful resection of the duodenum and a portion of the pancreas for carcinoma involving the ampulla of Vater and the head of the pancreas. Since that date, 14 cases have been reported in the literature and one of us (T. G. O.<sup>6</sup>) has just reported the fifteenth case. This patient is alive and well eight months after the resection. Whipple<sup>7</sup> reported one patient who was alive and well, with a gain of 30 pounds in weight, two years after the original operation.

In 1934, Hunt and Budd<sup>8</sup> collected 76 cases of radical extirpation of carcinoma involving the periampullary region, with an operative mortality of 38 per cent. They estimated that 85 such cases had been recorded, but they were unable to accurately verify this estimate. From 1925 to 1934, these authors found recorded cases of transduodenal excision which lived three, five, and eight years after operation, respectively. Thus, radical resection has altered the rapidly fatal outcome of the disease when it has been treated in its early stages.

Renewed interest in this problem has led us to review the cases which appear in the records of the University of Kansas Hospitals during the past 20 years. In addition to 35 cases of primary carcinoma of the pancreas, 17 cases of carcinoma of the ampullary region were also reviewed because of the similarity of symptoms produced and because in their early stages they are amenable to similar surgical treatment. Only those cases proven by autopsy or surgical biopsy are included in this analysis.

## CARCINOMA OF THE PANCREAS

*Incidence.*—Carcinoma of the pancreas is a condition found most frequently in the fifth and sixth decades of life. All our patients were between ages 46 and 78. Three patients were in their late forties, 13 in their fifties, 15 in their sixties, and four were in their seventies. Thirty-two of the patients were white and three were colored. Other series reported by D'Aunoy, *et al.* (40 autopsy cases), Lahey and MacKinnon (47 cases), and Grauer<sup>9</sup> (34 autopsy cases), also indicate that the disease occurs anywhere from ages 26 to 80, but that it is most frequent in the fifth and sixth decades of life. Although primary carcinoma of the pancreas is exceedingly rare in persons under 20 years of age, the literature contains reports of about nine proven cases. Mielcarek<sup>10</sup> collected five proven cases from the literature up to 1935. The youngest was an infant age 7 months. He reported the sixth case which occurred in a boy age 15. He listed five other cases from the literature as doubtful because they lacked proof. Since then, Smith<sup>11</sup> reported one case in a boy age 14½, Jeanneney and Laporte<sup>12</sup> one case in a girl age 17, and Kaletcheff<sup>13</sup> a case in a girl age 14. The ratio of incidence in the male and female varied from 17:1 in D'Aunoy's series to 23:24 in Lahey's series.

*Pathology.*—In almost all of our cases, the tumor was hard and scirrhous. In two instances, a soft medullary tumor was found. The tumors arose from the acini in the majority of the patients. In five cases, definite indication that it arose from pancreatic duct epithelium was found. In 25 cases, the tumor involved the head, in seven, the body, and in three cases, the whole pancreas was involved in an extensive growth.

*Symptoms.*—The symptoms complained of were mild and of recent duration at the time that the patients presented themselves at the hospital. The duration of the symptoms varied from one to nine months. Only five patients complained of vague abdominal symptoms of two to five years' duration. The most frequent complaints were vague abdominal discomfort, indigestion, gas, and dyspepsia. Rapid weight loss and weakness were complaints in 85 per cent of the cases. Jaundice was present in 17 of 23 cases of cancer of the head of the pancreas, and was reported as being present in 22 of 31 patients in D'Aunoy's series. In two cases, the jaundice was intermittent while in 15, it was severe and progressive. Jaundice was not present in any of the cases of carcinoma of the body of the pancreas. Symptoms of duodenal obstruction occurred in seven instances and duodenal ulceration in three. Gas was one of the chief complaints in 15 patients, absent in five, and not complained of by the other 15 patients. In the majority of cases, pain was mild and vague in character. In 16 patients, it was localized to the mid-epigastrium, in three, to the right upper quadrant, in two, to the back only, and in four, to the epigastric region and back, and in one case, to the right shoulder blade. The pain was severe and sharp in only two cases. In one case it was severe and colicky. The colicky pain in the latter patient probably came from the biliary passages because he also had an intermittent jaundice. Pain was not complained of by two patients. This is in contrast to the

## CARCINOMA OF THE PANCREAS

conclusion of Kauer and Glenn, who found that pain was the most common chief complaint in 68 per cent of their patients. The pain in the patients with carcinoma of the body of the pancreas did not differ in severity from that of the head of the pancreas. Archibald and Kaufman<sup>14</sup> describe the pain in carcinoma of the body of the pancreas as being extremely severe and destroying in character in contrast to the vague pain in carcinoma of the head and tail of the pancreas. In their analysis of 19 cases of primary carcinoma of the body and tail of the pancreas, Levy and Lichtman<sup>15</sup> report a wide variation in the reference and type of pain complained of. Occasionally, it would simulate gallbladder disease or penetrating ulcer but it was unrelated to the digestive cycle.

A palpable abdominal tumor was found in 23 of our 35 cases. In ten patients, it was located in the region of the gallbladder; in eight, it was mid-epigastric; in two, it was at the umbilicus; and in three, it was felt in the left epigastric region. In the latter three cases, the tumor involved the body of the gland. Ascites was present in three patients.

Twenty-seven of the patients were explored and palliative operations were performed. Cholecystogastrostomy was performed in six cases, and cholecystostomy in one case, to relieve biliary obstruction. Gastro-enterostomy was performed in six cases, and duodenojejunostomy in one case, to relieve duodenal obstruction.

Early, extensive metastases were observed to be the rule. These were noted at the time of operation and at autopsy. Metastases involved the adjacent lymph nodes, liver, and lungs. Extension of the growth by contiguity to the mesentery, peritoneum, and adjacent organs was frequent.

*Mortality.*—Carcinoma of the pancreas was a rapidly fatal condition in our patients. The duration of symptoms was short in the majority of the patients and varied from one to nine months. In all of our patients, death occurred two to ten months after the onset of symptoms, and from two and one-half to five months after the onset of progressive jaundice. All of the patients upon whom palliative operation was resorted to for relief of biliary or duodenal obstruction died within five weeks after the operation. D'Aunoy, *et al.*, reported the duration of illness in 38 of their 40 cases to be one to eight months, with an average of four and one-half months.

## CARCINOMA OF THE AMPULLA OF VATER

We have reviewed 17 proven cases of carcinoma of the ampullary region. Three of the lesions were fungative and had undergone mucoid degeneration. Ten of the patients were men and seven were women. Three were in their forties, four in their fifties, seven in their sixties, and three in their seventies.

The symptoms were mild and were present two to 15 months at the time of admission, with an average duration of four months. Vague epigastric discomfort, nausea, vomiting, anorexia, weakness, and rapid loss of weight were the chief symptoms. Progressive jaundice unassociated with severe

pain was present in all patients. A palpable, right upper quadrant mass was felt in four patients.

Operation was performed in 16 instances. Biopsy only was done in four cases, cholecystogastrostomy was performed in six patients, cholecystectomy in one, and cholecystoduodenostomy in one patient. This latter patient lived 33 months after cholecystoduodenostomy for an obstructive lesion of the ampulla. A hard nodule in the head of the pancreas was felt at operation but no biopsy was obtained. Autopsy after death showed an adenocarcinoma of the ampulla of Vater. It is entirely possible, but not likely, that this patient had a benign obstruction which was relieved by operation and that he subsequently developed an ampullary malignancy. Choledochogastrostomy and resection of the head of the pancreas and duodenum was performed in one patient. This patient is still alive and in good condition, eight months after operation. The average duration of life from the onset of the symptoms was five months (two to nine months). The growths extended up into the bile ducts, to the pancreas and duodenum, and metastasized to the liver, lungs, and ovaries.

*Fatty Infiltration and Degeneration of the Liver.*—Eight of our 35 cases of carcinoma showed definite fatty metamorphosis of the liver at autopsy. A brief summary of the individual cases is charted in Table I.

TABLE I  
FATTY INFILTRATION AND DEGENERATION OF THE LIVER IN PATIENTS WITH  
CARCINOMA OF THE PANCREAS AND AMPULLARY REGION

Case No.	Age	Sex	Duration of Symptoms (Mos.)	Duration of Jaundice (Mos.)	Location of Carcinoma	Changes in the Pancreas
1	57	M.	5	3	Head	Generalized atrophy of pancreas Chronic pancreatitis
2	51	F.	1	1	Head	Chronic fibrous pancreatitis
3	62	M.	4	0	Body	Extensive carcinoma of body of pancreas
4	59	M.	8	0	Head	Extensive carcinoma of head of pancreas
5	57	F.	5	0	Body	Chronic interstitial pancreatitis
6	61	M.	2	2	Head	
7	75	F.	9	0	Head	Chronic pancreatitis
8	71	M.	6	0	Head	Fibrosis of pancreas
9	60	M.	15	3	Ampulla	Chronic pancreatitis
10	55	M.	6	1½	Ampulla	Chronic cystic pancreatitis

The rôle of the pancreas in controlling the endogenous metabolism of fat, particularly in the liver, was suggested by early experiments upon dogs. In 1924, Fisher,<sup>16</sup> and also Allan, Bowie, MacLeod, and Robinson<sup>17</sup> reported that life could be maintained in totally pancreatectomized dogs for only one to 11 months, even though the blood sugar was controlled by daily administration of insulin. At death, the greatest change was observed in the liver. There was marked fatty infiltration and degeneration. The fat content of the liver increased to 39.5 per cent. These observations were subsequently confirmed in experiments on dogs by Hershey<sup>18</sup> (1930).

Conflicting experimental evidence is found in the literature as to whether fatty metamorphosis of the liver can be produced by loss of pancreatic secretion through total pancreatic fistula and by ligation of the pancreatic ducts. In 1931, Berg and Zucker,<sup>19</sup> and Hershey reported the development of fatty livers in dogs following the loss of pancreatic juice by total external pancreatic fistula in from 17 to 56 days. Excessive fatty infiltration of the liver also occurred after prolonged obstruction of the pancreatic ducts (80 days) by ligation. Van Prohaska, Dragstedt, and Harms<sup>20</sup> found fatty livers in three of their seven dogs with pancreatic fistula, but ascribed this occurrence to intercurrent infection which developed in these three dogs. Two had a subcutaneous abscess, and one died from peritonitis. The other four dogs had normal livers. Two of their three dogs with ligated pancreatic ducts showed fatty livers, the third did not. In spite of these observations, they concluded that fatty degeneration of the liver does not occur in dogs with total pancreatic fistula and in dogs with ligated pancreatic ducts. Boyce and McFetridge<sup>21</sup> present evidence which indicates that fatty changes in the liver develop after complete or partial pancreatectomy but do not occur when the pancreatic ducts are severed and ligated with the pancreas left *in situ*. Ralli, Rubin, and Present<sup>22</sup> repeated these experiments on dogs in 1938, in an attempt to clarify this controversy. They found that careful ligation of the pancreatic ducts and separation of the pancreas from the intestine in three dogs produced fatty changes in the livers which were indistinguishable from those of pancreatectomized dogs.

Thus, some investigators maintain that their evidence indicates that the external secretion of the pancreas contains the factor necessary for the control of fat metabolism in the liver. Others do not agree with this contention. Feeding of pancreatic juice and administration of extracts of pancreatic juice did not prevent or cure the fatty changes in the experiments of Van Prohaska, *et al.*, and of Dragstedt.<sup>24</sup> One hundred grams of raw pancreas added to the daily diet was effective in preventing the fatty degeneration. Hershey found that substitution of 10 Gm. of lecithin for raw pancreas in the daily diet also maintained normal liver fat. Best, Ferguson, and Hershey<sup>23</sup> found that adding choline to the diet in amounts equal to that present in 10 Gm. of lecithin protected the animal. This indicated that the active principle in lecithin is choline. Dragstedt summarized the results of three years' investigation of the problem in 1940. He pointed out that 100 Gm. of raw pancreas fed daily is effective in protecting the liver and that it contains only 250 mg. of choline, whereas 2 Gm. of choline a day or more is necessary. He also states that the lecithin in the raw pancreas is specific. Feeding liver or brain which contains a lot more lecithin and choline exerts no beneficial effect. He has prepared an active alcohol soluble extract of beef pancreas 60 to 100 mg. of which are effective by mouth and subcutaneously. The extract is free from fat and contains only 1 to 2 per cent choline. He concludes that this substance is specific and active in small amounts, and is not choline, but a new pancreatic hormone which he has termed "lipocaic."



The foregoing experimental evidence indicates that the pancreas is concerned with the endogenous metabolism of fat in the liver. Fatty infiltration and degeneration of the liver occurs following total pancreatectomy, and also may follow a loss of pancreatic juice in total fistula and following ligation of the pancreatic ducts. This fatty metamorphosis of the liver can be prevented in the dog by feeding raw pancreas (100 Gm. daily), and, according to some workers, lecithin (10 Gm. daily), choline (2 Gm. daily), and lipocaic (60 to 100 mg. daily). The fact that fatty liver follows ligation of the pancreatic ducts in some instances does not mean that it is due to a loss of pancreatic juice. It may well be due to a decrease in lipocaic below the maintenance level, because of fibrosis of the pancreas and degeneration of lipocaic producing parenchyma. The same may be true following chronic pancreatitis and fibrosis in the case of total pancreatic fistula. Cole<sup>25</sup> has called attention to fatty infiltration of the liver associated with pancreatic fibrosis. Snell and Comfort<sup>26</sup> report cases of pancreatic lithiasis and atrophy as probable causes of fatty changes in the liver. Our ten cases show that fatty infiltration and degeneration of the liver can occur with pancreatic insufficiency due to cancer involvement of the pancreas. In most of the cases presented, the carcinoma involved the ducts and produced obstruction, secondary atrophy, and chronic inflammation of the pancreas. In some instances, most of the gland was replaced by cancer. If fatty metamorphosis of the liver is due to extensive functional destruction of the pancreas, one might expect to have an associated diabetes. None of our patients had glycosuria or hyperglycemia. Reports of infrequent cases of diabetes with cancer of the pancreas have been recorded by Uhry,<sup>27</sup> and by Pygott and Osborn.<sup>28</sup> Apparently, in our patients protection against fatty metamorphosis of the liver required more pancreatic tissue than was needed to prevent diabetes. On the other hand, the fatty infiltration of the liver observed in our patients may be due to a loss of the external pancreatic secretion due to obstruction of the pancreatic ducts, as occurred in the dogs of Berg, *et al.*, Van Prohaska, *et al.*, and Ralli, *et al.* Regardless of the mechanism involved, experimental evidence and the presence of fatty livers in ten of our patients warrants the administration of lecithin (10 Gm. daily), choline (2 Gm. daily) or lipocaic (100 mg. daily) to patients with pancreatic insufficiency, both preoperatively and postoperatively.

The rapidly fatal course of the disease in our series, and in the other series reported in the literature, does not offer much hope for patients with carcinoma of the pancreas or ampullary region. The few successful resections reported within the past seven years bring some hope if the lesion is discovered early. In most instances, however, patients do not seek medical help until jaundice or marked loss of weight has occurred, during which time extensive metastases have already developed, so that death follows shortly after they are seen.

An early diagnosis may be hoped for in the future by a thorough investigation of the pancreas in all cases of inexplicable abdominal pain, rapid

## CARCINOMA OF THE PANCREAS

weight loss, nausea, and jaundice. Stools should be analyzed for their fat after several days of a standard diet of known fat content. Samples of duodenal juice should be obtained by intubation and analyzed for pancreatic ferments. Blood amylase and lipase, which are elevated in obstructions of the pancreatic ducts, may be suggestive. Carcinoma of the body or tail of the pancreas may not produce any detectable loss of the external secretion of the gland. In many cases, the pain may also be vague and mild so that early diagnosis is extremely difficult or impossible without operation. Gastroscopic examination may be of some diagnostic value but only after the tumor has grown to a large size. Moersch and Comfort<sup>29</sup> report gastroscopic examination in two cases of carcinoma of the body of the pancreas in which the tumor caused a bulging of the stomach wall, which could not be obliterated by inflation of the stomach with air.

An exploratory operation is justified even in advanced cases. In early lesions involving the ampulla and head of the pancreas, radical resection is the procedure which gives the only hope of cure to the patient. In advanced cases, palliative operations for relief of biliary or duodenal obstruction are indicated to increase the comfort of the patient during the last stages of the disease. In spite of the fact that all of our patients, except one, died within five weeks of the palliative operation, such treatment is indicated because in some instances the patient's life may be greatly prolonged, as shown by our case noted above of a man age 60 who lived 33 months after palliative cholecystoduodenostomy for carcinoma of the head of the pancreas. This case was confirmed at autopsy. Coughlin and McCaughan<sup>31</sup> also report prolonged survivals in three patients following cholecysto-enterostomy for tumor of the head of the pancreas; one was alive at three months, one at 14 months, and one at five years, respectively.

### CONCLUSIONS

(1) An analysis of the problem of carcinoma of the pancreas and ampullary region is made from a study of 52 patients, with a proven diagnosis by autopsy or biopsy.

(2) The rapidly fatal course of the disease, in most of the patients, is pointed out.

(3) Thorough investigation of pancreatic function is advisable for the diagnosis of an early obscure cancer of the pancreas or ampulla of Vater in all cases of inexplicable abdominal complaints.

(4) Radical resection, by the technic of Whipple or that of Hunt and Budd, offers the only hope for cure of early carcinoma of the ampullary region or the head of the pancreas. Palliative operation for relief of biliary or duodenal obstruction, even in advanced cases, is indicated, not only to make the patient more comfortable but to prolong life.

(5) Fatty infiltration and degeneration of the liver was found at autopsy in ten of our 52 patients with carcinoma of the ampulla and head of the pancreas. We have tried to explain this on the basis of the experimental

evidence found in the literature, which is reviewed. The feeding of lecithin, choline, pancreatic extract, or lipocaic is indicated in the preoperative and postoperative treatment of these patients to prevent fatty changes in the liver and to maintain life.

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## THE RATIONALE OF RADICAL SURGERY FOR CANCER OF THE PANCREAS AND AMPULLARY REGION\*

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UNTIL 1935, pancreaticoduodenectomy for cancer involving the pancreas was not attempted for the following reasons: (1) The duodenum was believed to be an essential part of the digestive tract. (2) The external secretion of the pancreas was believed to be indispensable for digestion of proteins and fats. (3) The significance of the fact that pancreatic juice ceases to flow and that acinar atrophy results with prolonged blockage of the ampulla and head of the pancreas with carcinoma was not properly understood or evaluated. (4) For these reasons, even with resections of part of the duodenum, every effort was made to reestablish the flow of bile and pancreatic juice into the duodenum or jejunum.

Halsted,<sup>1</sup> in 1898, was the first to carry out such an operation successfully. Doctor Hunt has summarized the collected cases of this type, some 110 in the literature and by personal communication. Because the unsuccessful operations have not been reported, the results are somewhat misleading in evaluating the collected cases, both as to operative mortality and the late results.

Nevertheless, for carcinoma limited to the papilla of Vater, transduodenal resection with reimplantation of the common and pancreatic duct into the duodenum offers definite advantages and this is especially true of the fungating or papillary type of carcinoma of the ampulla.

But not all cancers of the ampulla are of the fungating type, nor are all of the fungating growths relatively benign. Many of them infiltrate either the pancreas or the common duct, or the duodenum. Attempts to excise a segment of the head of the pancreas, wide of the growth, with a reimplantation of the ducts or head of the pancreas into the duodenum or jejunum have, in many instances, been associated with fatal hemorrhage, peritonitis, or duodenal fistula. This is especially true if catgut is used for ligatures and sutures. The activated pancreatic juice rapidly digests catgut. Surgeons, in the past, have hesitated to use silk or cotton because they considered the duodenum a contaminated field.

Following the fatal outcome, due to duodenal fistula and peritonitis, in a transduodenal excision of an ampullary carcinoma which I performed in 1935, we decided to undertake a more radical operation in two stages for the following reasons: (1) Coffey,<sup>2</sup> in 1909, and Mann and Kawamura,<sup>3</sup> in 1922, had demonstrated that the dog could survive total duodenectomy. (2) Patients with ampullary or pancreatic cancer were able to survive for months

\* Discussion of Dr. Verne Hunt's paper read at the meeting of the American Surgical Association, White Sulphur Springs, W. Va., April 28, 1941.



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TABLE I  
FORTY-ONE COLLECTED CASES OF RADICAL PANCREATODUODENECTOMY FOR CARCINOMA  
(Collected from the Literature and from Personal Communications)  
To April 15, 1941

Operator	Reported in Journal	Stage	Ampul- lary	Pan- creas	Duo- denum	Com- mon Duct	Died Post- oper.	Died After Opera- tion	Surviving	Ca. with Metas- tases	Recur- rence	Fis- tula Post- oper.
1. Parsons.....	ANNALS OF SURGERY, 102, 763, 1935	2	x					9 mos.				
2. Whipple.....	ANNALS OF SURGERY, 102, 703, 1935	2		x				28 mos.		x		
3. Whipple.....	Amer. Jour. Surg., 40, n.s., 260, 1938	2						5 mos.				
4. Schullinger-Parsons..	Amer. Jour. Surg., 40, n.s., 260, 1938	2		x			x					Biliary Pancreatic
5. Jasssen-Whipple.....	Amer. Jour. Surg., 40, n.s., 260, 1938	2		x			x		15 mos.			
6. Whipple.....	Not reported	21		x			x		15 mos.			
7. Whipple.....	Not reported	21		x			x		15 mos.			
8. Whipple.....	Not reported	1		x			x		15 mos.			
9. Whipple.....	Not reported	1		x			x		15 mos.			
10. Trout.....	Personal communication	1			x		x					
11. James.....	Personal communication	2					x		2 mos.			
12. James.....	Personal communication	2					x		35 mos.		x	
13. Hollenberg.....	Personal communication	2							5 mos.			
14. Orator.....	Zentralblatt f. Chir., 64, No. 25, 1936	2										
15. Crile, Jr.....	Am. Jour. Surg., Jan., 1940	2		x				18 mos.				
16. Zimniger.....	Personal communication	21	x					17 mos.				Pancreatic Biliary
17. Zimniger.....	Personal communication	21	x					4 mos.				
18. Zimniger.....	Personal communication	1		x				3 mos.				
19. Watt.....	Personal communication	2		x				5 wks.				
20. Ellingworth.....	Edinburgh Med. Jour., 46, 331, 1939	2		x				3 mos.				
21. Powers.....	Personal communication	1		x				11 mos.				
22. Trimble.....	Personal communication	2		x				15 mos.				
23. Lake.....	Personal communication	2						6 wks.				
24. Pfeiffer.....	Personal communication	2						5 mos.				
25. Horsley.....	In print. ANNALS OF SURGERY, 1941	1	x				x					
26. Jones.....	Personal communication (Crile)	2		x				5 mos.				
27. Freeman.....	Personal communication	2		x				11 mos.				
28. Freeman.....	Personal communication	2		x				1 mo.				
29. Freeman.....	Personal communication	2						6 mos.				
30. Fallon.....	Personal communication	2						2 mos.				
31. Fallon.....	Personal communication	2						1 wk.				
32. Fallon.....	Personal communication	21		x				2 mos.				
33. Fallon.....	Surge., Gynec. and Obstet., 65, 681, 1937	1		x				1 wk.				
34. Brunschwig.....	Personal communication	2						3 mos.				
35. Brunschwig.....	Personal communication	2						3 mos.				
36. Braunschwig.....	Norsk. Mag. f. Laegevid., 98, 777, 1937	2		x			x					
37. Roscher.....	Personal communication (Hunt)	2						5 mos.				
38. Ransom.....	Tr. West. Surg. Assn., 1940	2						7 mos.				
39. Ott.....	Personal communication	2						1 yr.				
40. Hunt.....	Personal communication	1										
41. Hunt.....	Personal communication	2										

<sup>1</sup> A modified two-stage procedure.

**RÉSUMÉ OF MORTALITY INCIDENCE  
FOLLOWING RADICAL OPERATIONS FOR CARCINOMA, WITH RESECTION OF  
DUODENUM AND PANCREAS**

*Collected Cases to April 15, 1941*

	Two- Stage	Postop. Deaths	One- Stage	Postop. Deaths
Carcinoma of ampulla.....	16	2	4	2
Carcinoma of pancreas.....	14	7	2	0
Carcinoma of duodenum.....	2	1	1	0
Carcinoma of common duct.....	2	0	—	—
Totals.....	34	10	7	2
Total operated cases.....	41			
Postoperative deaths.....	12			
Operative mortality.....	29. 2%			

deprived of both biliary and pancreatic contents in the gastro-intestinal tract, and showed an atrophy of disuse of the acinar tissue of the pancreas. (3) If bile could be restored by a short-circuiting procedure, the bleeding tendency would be corrected and digestion of fat improved. At the same operation a gastro-enterostomy would prepare the patient for the second stage, at which time radical removal of the duodenum and head of the pancreas, wide of the growth, would be undertaken.

Doctor Parsons and I<sup>4</sup> operated upon the first patient, employing the two-stage procedure, in 1935. At the second stage, a partial duodenectomy with excision of part of the head of the pancreas, with duodenoduodenostomy, but with exclusion of the pancreas from the digestive tract, was accomplished. In the second case I<sup>4</sup> performed a total duodenectomy, with excision of a part of the head of the pancreas. The patient lived 28 months, but died of liver metastases. Both of these patients digested 80 to 85 per cent of a measured fat intake, on several determinations. But both of them developed cholangitis because of the cholecystogastrostomy.

Because of the tendency for infectious material to be pushed into the gall-bladder and the development of a stenosis of the stoma with biliary infection, we<sup>5</sup> modified the short-circuiting procedure in the first stage to an end-to-end cholecystojejunostomy, with an end-to-side jejunojejunostomy. In some 31 such operations (the great majority of them palliative), we have found a very low incidence of cholangitis, and now strongly advise it as a first-stage procedure, rather than a cholecystogastrostomy.

But the two-stage procedure, as reported in the literature, and in personal communications to me by surgeons who know of my interest in the subject, carries with it certain hazards and complications which must be eliminated if the radical operation is to be considered worth while. The two most serious complications are postoperative bile and pancreatic fistula. In the 41 collected cases, there have occurred five bile and eight pancreatic fistulae (Table I). The former seldom close spontaneously, the latter usually do. The bile fistula is due to the cutting through of the silk or linen ligature used in tying off the common duct in the second stage. If possible, it is, undoubtedly, better

policy to implant the end of the common duct into the jejunum. Pancreatic fistula can be avoided by ligating the dilated pancreatic ducts before approximating the cut surfaces of the V-shaped excision in the head or body of the pancreas.

Now that we can prepare jaundiced patients for operations with vitamin K and bile salts, and can prevent shock by adequate measures, it is possible, in early and in selected cases, to undertake the radical operation in one stage. This avoids the hazard of two anesthetics and two major procedures.

I performed the first successful one-stage radical pancreaticoduodenectomy in March, 1940, removing the distal third of the stomach, the entire duodenum, and the head of the pancreas with an antecolic gastrojejunostomy and a choledochojejunostomy. This 47-year-old woman has regained 20 pounds, and is now living and free from any signs of jaundice or recurrence, 14 months after operation. The second patient upon whom I performed a similar one-stage procedure, in September, 1940, died of a postoperative pneumonia on the fourth day.

Fine silk technic should be used in all pancreatic surgery. Some of these patients will show a poor fat digestion, others good digestion. We are carrying out a series of experiments to explain this discrepancy. Pancreatic extract should be given to those who show fat indigestion. In our patients who have died following the radical two-stage procedure, we have not found fatty liver degeneration. However, it may be wise to give these patients lipocaic after operation.

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## ANASTOMOSIS OF THE BILE DUCTS TO THE GASTRO-INTESTINAL TRACT BY A METHOD OF TRANSFIXION NECROSING SUTURE\*

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ANASTOMOSIS between the bile ducts and the gastro-intestinal tract may result in cicatricial stenosis of the stoma,<sup>a†</sup> with resulting increase of intra-ductal pressure, stasis of the bile, dilatation of the biliary tree and ascending infection of the ducts and liver,<sup>b†</sup> with resulting liver damage. A large stoma at the site of anastomosis frequently results in regurgitation into the biliary system<sup>c†</sup> of pancreatic juice, food and bacteria, with resulting liver damage, as evidenced by liver enlargement,<sup>d†</sup> dilatation of the bile ducts, liver necrosis and infection. The immediate mortality and late results of the performance of such an anastomosis depend also on the damage to the liver at the time of operation,<sup>e†</sup> the biliary ductal segment available for use, as well as upon the difficulty and uncertainty of the anastomosis performed.<sup>116</sup>

Whipple,<sup>120</sup> in 1928, stated that "the rare successes not the many failures appear in the literature." Evarts Graham,<sup>46</sup> in 1938, stated that "almost invariably the patient succumbs from multiple abscesses in the liver if the anastomosis remains open." Arthur Allen,<sup>1</sup> in 1940, stated that "one wishes to avoid, if possible, anastomosis between the duct and the gastro-intestinal tract, since under these circumstances an ascending infection is so apt to occur." Waltman Walters,<sup>116</sup> in 1939, stated that "life has been prolonged by operation to 25 per cent of the normal expectation."

The principles involved in the selection of a site in the gastro-intestinal tract for anastomosis to the biliary system concern themselves with the accessibility and motility of the duodenum,<sup>f†</sup> the low potential of infection in the stomach, which is somewhat modified by the gross character of its contents and its anatomic disparity,<sup>g†</sup> and the universal motility of the jejunum.<sup>68, 123</sup> During exposure of the duct,<sup>116</sup> preservation of the peritoneum,<sup>h†</sup> periductal tissues, nerve and blood supply of the duct is important.

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

<sup>a†</sup> References in this group are: 17, 24, 30, 59, 66, 70, 80, 84, 86, 90, 96, 104, 107, 116, 118, 119, 122, 123.

<sup>b†</sup> References in this group are: 1, 31, 43, 60, 62, 63, 65, 66, 69, 80, 104, 119, 121.

<sup>c†</sup> References in this group are: 9, 14, 15, 29, 31, 44, 55, 70, 81, 98, 108, 112, 123.

<sup>d†</sup> References in this group are: 70, 99, 109, 123.

<sup>e†</sup> References in this group are: 86, 111, 116, 123.

<sup>f†</sup> References in this group are: 59, 73, 123.

<sup>g†</sup> References in this group are: 10, 47, 59, 70, 73, 102, 123.

<sup>h†</sup> References in this group are: 18, 75, 89.

The reported methods and cases of cholangio-enterostomy are numerous.<sup>1†</sup> Gaston,<sup>39</sup> in 1885, reported anastomosis between the gallbladder and duodenum by a suture, as follows<sup>2</sup>: "Sufficient inflammation ensued from a single stitch of silk thread to unite the walls, while it cut an opening between these cavities which closed in five months in one dog, but in this the common duct had not been ligated below. No obstruction or infection in the biliary tree, the viscera had not had an inflammation propagated from the suture to the attached walls." Gage<sup>37</sup> found histopathologic changes in all of 40 normal dog livers, which consisted of round cell infiltration, small areas of necrosis, and small abscess-like areas; after choledochoduodenostomy, 46.6 per cent showed increase in the pathologic changes after 15 days. Sandblom, Bergh, and Ivy<sup>101</sup> stated that "the site of anastomosis does not affect the problem of ascending liver infection." These authors anastomosed the gallbladder to the duodenum after pyloric exclusion and ascending liver infection occurred. Gentile<sup>42</sup> found that ascending liver infection occurred after gastric resection and cholecystogastrostomy.

Bernhard<sup>14</sup> reported the finding of roentgenologic evidence of regurgitation of stomach contents into the liver after anastomosis between the gallbladder and gastro-intestinal tract. Ellsworth Eliot<sup>31</sup> stated that "the fear of infectious cholangitis has been dissipated by the instances of barium, introduced into the stomach, which has been found to penetrate the hepatic tributaries with no indication of even mild cholangitis."

Mallet-Guy,<sup>70</sup> in 1940, stated that "in the dog, after choledochoduodenostomy, pancreatic reflux often causes liver necrosis. The presence of air in the biliary tree is common and the incidence of barium reflux is great." McWhorter<sup>81</sup> reported a case seven years after hepaticoduodenostomy, with liver enlargement, in which barium regurgitated into the biliary tree. Wildegans<sup>123</sup> observed that there had been numerous cases in which barium was evident in the branches of the hepatic duct after choledochoduodenostomy.

Beaver and Mann,<sup>12</sup> Berg,<sup>7</sup> Coffey,<sup>25</sup> Walton,<sup>118</sup> and perhaps others, placed the end of the common bile duct into the lumen of the duodenum and found universal dilatation of the biliary tree. Bachrach and Fogelson<sup>9</sup> found that when the common duct was pulled into the lumen of the jejunum through a stab wound and anchored to the distal wall, seven out of 13 animals lived for two to two and three-quarter years; there was regurgitation of barium in one and moderate ductal dilatation with negligible pathologic changes in the liver. These authors also found that bile peritonitis and later common duct obstruction followed when the common duct was fastened to the jejunum by sutures and the jejunal wall invaginated about the duct with a purse-string.

Anastomosis between the bile ducts and the gastro-intestinal tract in which transplanted tissues are used result in cicatricial stenosis, as shown by Horsley.<sup>53</sup> Anastomosis by suturing the duct and gastro-intestinal tract over

<sup>1†</sup> References in this group are: 9, 12, 16, 24, 25, 31, 32, 35, 36, 38, 39, 45, 48, 49, 50, 52, 53, 58, 59, 65, 67, 69, 70, 71, 74, 76, 78, 79, 80, 83, 84, 88, 92, 99, 102, 104, 105, 106, 111, 116, 120, 123, 125.



a rubber tube, or the use of a rubber tube to bridge a gap between the two, was performed by Brewer,<sup>21</sup> Cahen,<sup>24</sup> Fowler,<sup>35</sup> Mayo,<sup>78</sup> Jackson,<sup>58</sup> Mallet-Guy,<sup>70</sup> and Lahey,<sup>67</sup> with relatively poor results due to recurrence of stricture when the tube was removed and obstruction secondary to encrustations about the tube. Lahey stated that "the large majority of cases with rubber tubes have attacks of chills, jaundice and fever." McArthur<sup>79</sup> used a tube with a cuff on the duodenal end, and reported satisfactory late results in five cases.

A direct suture was first performed by Mayo<sup>75</sup> in two cases. Guerry<sup>50</sup> reported seven cases, with satisfactory results in four. Judd<sup>62</sup> anastomosed the hepatic duct to the duodenum by direct suture in 47 cases; there was contracture of the anastomosis in seven, after one to six months; also in another paper, Judd and Burden<sup>61</sup> reported 13 anastomoses of this type, with 15 per cent failures. Ladd and Gross<sup>65</sup> reported nine cases well after five to 16 years; these were instances of congenital stricture and atresia of the biliary tract. These authors stated "successful issue depends on care of doing anastomosis; it is not necessary to form a valve-like submucous transplantation. The mucous membrane of the duct and stomach or duodenum must be accurately opposed and no stenosis must exist." Eliot,<sup>31</sup> in 1936, collected, from the literature, 56 cases of hepaticoduodenostomy, and found 11 well after ten to 20 years. This author stated that "cholangitis is a frequent complication." Walters,<sup>116</sup> in 1939, reported 61 per cent of 80 operated cases of benign strictures of the common and hepatic duct anastomoses to the gastro-intestinal tract were performed, and 68 per cent obtained good results.

An external biliary fistula was transplanted to the gastro-intestinal tract in 41 cases collected by Eliot,<sup>31</sup> and five good results recorded. Contracture of the biliary fistula was found to be common. Lahey<sup>67</sup> stated that "several failures were due to repeated attacks of cholangitis."

*Operative Procedure.*—The principal feature of the method is the anastomosis of the bile duct to the gastro-intestinal mucosa by the necrosing effect of a No. 6 plain silk transfixion suture put through the ductal wall and gastro-intestinal mucosa (Fig. 1). The serosa and musculature of the gastro-intestinal tract are incised down to the submucosa. A medial or posterior row of mattress sutures which evert the edge of the gastro-intestinal incision around the duct are introduced through the peritoneum and connective tissue medial to the duct (Fig. 2). The transfixion suture is introduced into the duct for a distance equal to about two times the diameter of the normal duct, and the same length into the lumen of the gastro-intestinal tract. The duct wall and gastro-intestinal mucosa are crushed under pressure, by tying the transfixion suture. The operation is completed by suturing the everted anterior edge of the gastro-intestinal incision to the tissues lateral to the wall of the duct which places the duct in a covered submucous position in relation to the gastro-intestinal tract. This technic was employed in the experiments as well as the following variation: Figure 3 shows how, in the majority of the experiments, the sutures between the edges of the gastro-intestinal incision and the periductal tissues are introduced under the duct. In introducing these

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sutures at the most superior portions of the duct and the gastro-intestinal tract, the tissues at the side of the duct are employed for suturing, in order to avoid constriction of the duct (Fig. 4). The completion of the operation is similar to that shown in Figure 2.

*Results.*—Anastomosis between the common bile duct and the gastro-intestinal tract was performed by this technic upon 55 dogs. Deaths before

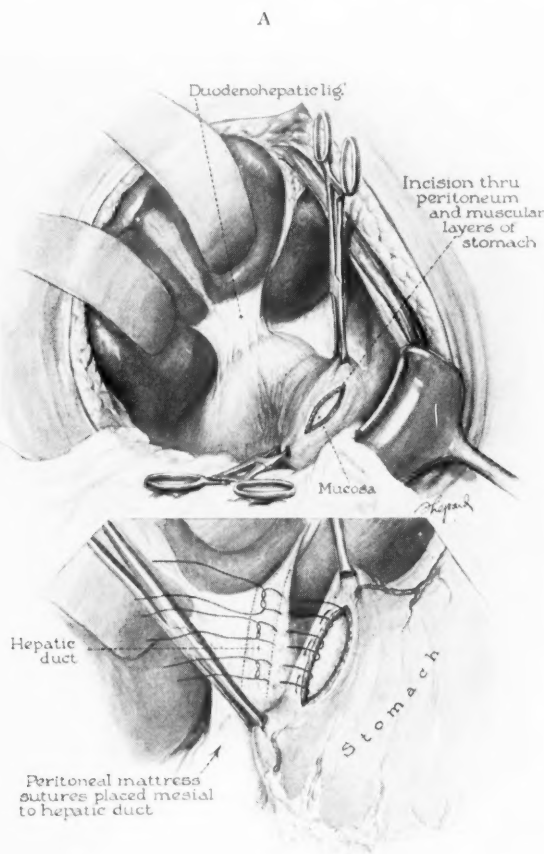


FIG. 1.—Anastomosis between the extrahepatic bile ducts and the stomach, in which technic the sutures between the duct and stomach do not pass under the bile duct. (A) Showing the duodenohepatic ligament, pylorus, and distal end of the stomach on the lesser curvature of which an incision has been made through the serosa and musculature layers. (B) Showing the bile duct lying beneath the peritoneum, mattress sutures between the undermined edge of the incision and the periductal tissue lateral to the duct are started on the serosal side of the stomach and the stomach and duct are approximated. Figure 2 shows the completed operation.

18 days were caused by pneumonia, in 12; jaundice, in 9; evisceration, in 3; leakage of anastomosis, in 2; rupture of hepatic duct, in 1; sponge under the liver, in 2; and causes unrelated to operation, in 2.

(A) *Effect of Type of Necrosing Suture.*—Anastomoses, using a silk transfixion necrosing suture, was established 38 times in 34 dogs (Figs. 5 and 6), living over seven days, with three exceptions which will be discussed later.

Four anastomoses using catgut, one using a strand of doubled silk, and one using heavy serum-proofed silk were not established.

(B) *Effect of Removal of the Peritoneum from the Bile Duct.*—Two simultaneous anastomoses (Fig. 7), of 1 cm. each, in six dogs, one through peritonealized duct and one through deperitonealized duct, resulted in all, through a peritonealized duct being established, and three, because of a deper-

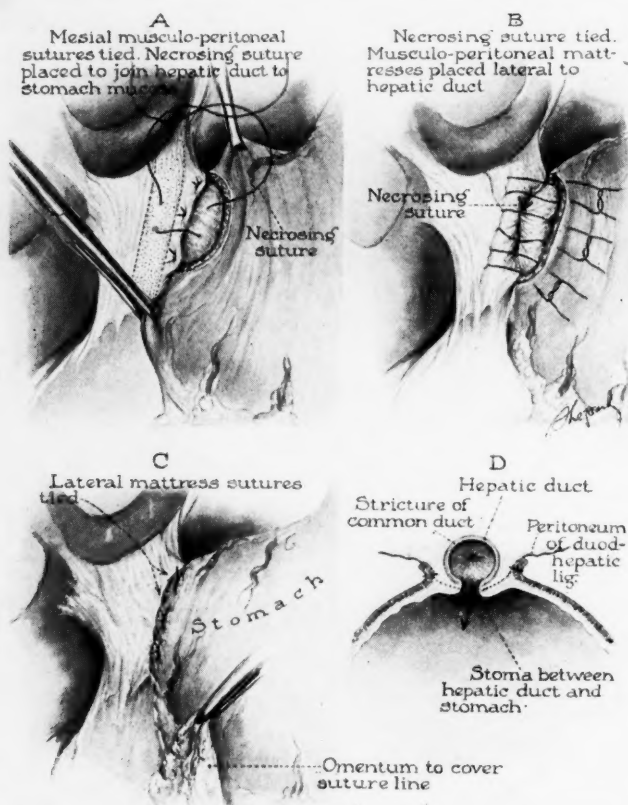


Fig. 2.—Continuation of anastomosis between the bile duct and the stomach (see Fig. 1). (A) Curved cutting needle on silk transfixion suture has been passed into the bile duct longitudinally, and into the lumen of the stomach through the gastric mucosa parallel to and equal in length to that in the bile duct, the posterior row of sutures (Fig. 1) has been tied, approximating the lateral edge of the duct and the posterior edge of the gastric incision. (B) Transfixion necrosing suture tied under pressure, and the musculo-peritoneal mattress sutures placed lateral to the duct are started on the gastric serosa, thus everting the undermined edge around the duct. (C) Lateral mattress sutures tied, thus covering the duct and gastric mucosa containing the transfixion necrosing suture; operation may be completed by suturing omentum over the suture line. (D) Sectional view showing bile duct in the wall of the stomach, peritoneum of the duodenohepatic ligament, looking distally down the bile duct toward the obstructive stricture in the duct, and the anastomotic stoma between the bile duct and the stomach. This technic was employed in some of the experiments reported and is less difficult to perform; both choledochoduodenostomy and choledochogastrostomy were performed in this way.

itonealized duct, failing to be established. These are the three failures mentioned previously.

(C) *Effect of Size of Anastomosis.*—An anastomosis of 1 cm. in eight dogs resulted in universal dilatation of ducts and regurgitation of intestinal contents with liver necrosis in 2, and liver abscess in 1. The anastomosis

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was 3 to 7 Mm. after one to 13 months. Deaths were due to pneumonia, in 3; emaciation, 2; liver abscess, 1; infected wound, 1; and one was sacrificed. The results are shown in the upper part of Table I.

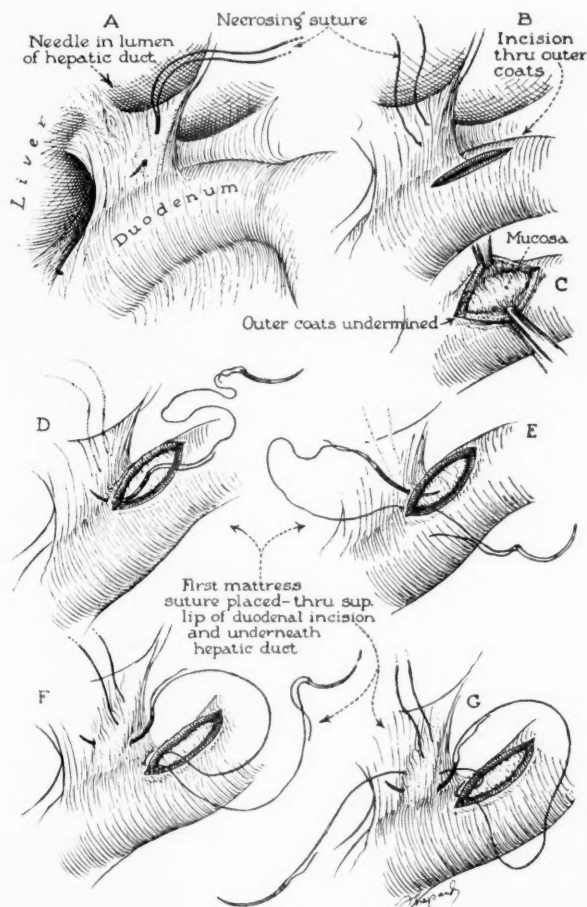


FIG. 3.—Anastomosis between the extrahepatic bile ducts and the duodenum. (A) Curved needle on silk transfixion necrosing suture has been placed into the lumen of the bile duct and out, producing a suture longitudinally in the duct, including duct wall and peritoneum overlying the duct. (B) Longitudinal incision through serosa and muscle of the duodenum. (C) Edges of incision undermined. (D, E, F, G) Showing insertion of mattress suture between the edge of incision and the region of the bile duct, suture is started on the serosal side to invert the incision around the duct, these sutures pass under the duct. Figure 4 shows completion of the anastomosis.

An anastomosis of 0.5 cm. in 13 animals resulted in the absence of pathologic changes in all, excepting ductal dilatation in 2, and slight liver necrosis in 1. The anastomosis was 5 to 3 Mm. after one to nine months. Deaths were due to pneumonia, in 4; hepatic failure, 1; and 7 were sacrificed. The results are shown in the lower part of Table I.

(D) *Effect of Immediate Section of the Common Duct Below the Anastomosis.*—The common bile duct was immediately sectioned below the anastomosis measuring 0.5 cm. in 23 dogs. In ten, living 18 days to nine months, this resulted in the absence of pathologic changes in all, excepting one showing

regurgitation and slight liver necrosis. Early deaths, before 18 days, were caused by pneumonia, in 10; jaundice, in 1; rupture of hepatic duct, in 1; and infected wound, in 1. Late deaths, 18 days to nine months, were caused by pneumonia, in 2; infected wound, 1; and 7 were sacrificed (Figs. 8 and 9).

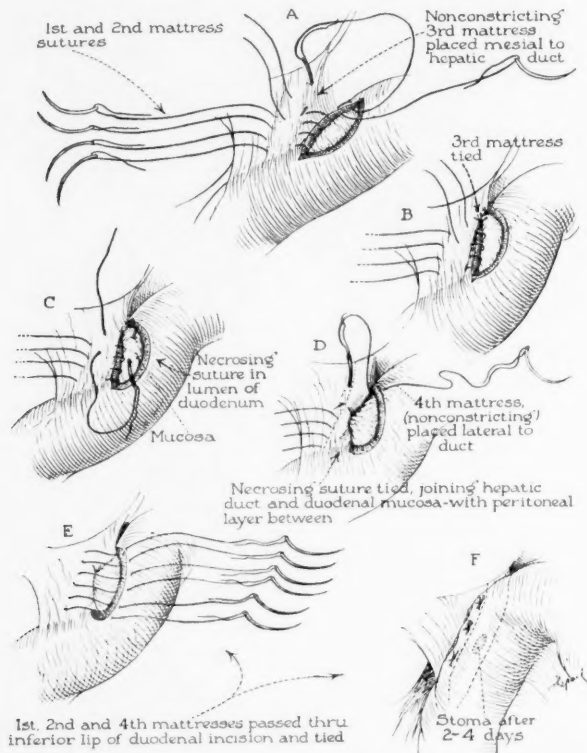


FIG. 4.—Continuation of anastomosis between the extrahepatic bile duct and the duodenum. (A) First mattress suture (Fig. 3), and second, have been placed, the third (B) is between the incision edge and the periductal tissue medial to the duct, to avoid stricture of the duct by the suture. (C) The transfixion necrosing suture which was placed into the duct (Fig. 3 A) has been put on a curved cutting needle and passed into and out of the lumen of the duodenum, catching the duodenal mucosa parallel to and equal to the length of suture already in the ductal wall. (B) The nonconstricting third mattress suture has been tied, approximating the duodenal incision and the medial side of the duct. (D) A suture similar to that shown in (A), is placed to approximate the upper part of outside edge of incision to lateral wall of bile duct. (E) Anastomosis is completed by passing the sutures through the free duodenal edge, tying, and thus covering the duct and transfixion necrosing suture which has been tied under pressure. (F) Completed operation showing submucosal position of bile duct and the immobilization of the duodenum and the approximate position of the stoma. This technic was employed in most of the experiments reported; both in anastomosis between the stomach and bile duct and between the duodenum and bile duct.

(E) *Effect of Site of Anastomosis in the Gastro-Intestinal Tract.*—An anastomosis of 0.5 cm. between the common bile duct and duodenum in ten animals resulted in absence of pathologic changes in all, except regurgitation and slight liver necrosis in one. The anastomosis was 5 to 3 Mm. after one to nine months.

An anastomosis of 0.5 cm. between the common bile duct and the stomach in three dogs, living one to three months, resulted in absence of pathologic



changes in all. The anastomosis was 3 Mm. (Fig. 10).

(F) *Effect of Type of Gastro-Intestinal Incision.*—A transverse gastro-intestinal incision was made in connection with the anastomoses of 0.5 cm. in three animals, living 18 days to five months, and resulted in liver necrosis and regurgitation in one.

A longitudinal gastro-intestinal incision was made in connection with the anastomoses of 0.5 cm. in 13 animals, living one to nine months, and resulted in the absence of pathologic changes in all (Fig. 11).

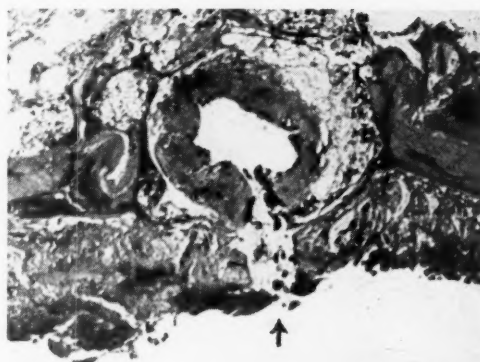


FIG. 5.—A photomicrograph of a cross-section of anastomosis between the common bile duct and the duodenum, taken 48 hours after operation. Necrosis of the ductal wall and duodenal mucosa, indicated by arrow, has occurred, demonstrating the early establishment of choledochoduodenostomy; to be compared to illustration (D) of Figure 2.

TABLE I

GROUP I. ANASTOMOSES OF ONE CENTIMETER					
No.	Mos.	Anastomosis	Regurgitation	Ductal Dilatation	Liver
9	1	5 Mm.	Positive	2 times	Normal
12	2	4 Mm.	Positive	4 times	Normal
7	3	6 Mm.	Positive	3 times	Necrosis
6	4	7 Mm.	Positive	2 times	Normal
2	4	5 Mm.	Positive	4 times	Abscess
5	6	6 Mm.	Positive	1 times	Necrosis
11	8	4 Mm.	Positive	1 times	Normal
1	13	3 Mm.	Negative	4 times	Normal
GROUP II. ANASTOMOSES OF ONE-HALF CENTIMETER					
13	1	5 Mm.	Negative	Negative	Normal
40	1	3 Mm.	Negative	Negative	Normal
55	1	3 Mm.	Negative	Negative	Normal
45	2	3 Mm.	Negative	Negative	Normal
35	2	4 Mm.	Negative	Negative	Normal
48	3	3 Mm.	Negative	Negative	Normal
44	4	4 Mm.	Negative	Negative	Normal
39	5	3 Mm.	Negative	Negative	Normal
33	5	5 Mm.	Negative	Negative	Normal
25	5	3 Mm.	Negative	Negative	Normal
15	5	3 Mm.	Positive	2 times	Necrosis
16	8	3 Mm.	Negative	Negative	Normal
32	9	3 Mm.	Negative	2 times	Normal

(G) *Effect of Removal of Gallbladder Together with Section of the Common Duct.*—The gallbladder was removed simultaneously with section of the common duct and the performance of an anastomosis of 0.5 cm. in three animals, living five to eight months, resulted in the absence of pathologic changes, in 2; and regurgitation and slight liver necrosis, in 1. The anastomosis was 3 Mm. (Fig. 12).

Preoperative cultures of gallbladder bile in 21 dogs resulted in three positive cultures. Postoperative cultures of gallbladder bile and of the liver in six dogs, one to nine months after anastomosis, resulted in all positive



FIG. 6.—A photograph of duodenal mucosa at the site of choledochoduodenostomy, 13 months after operation. The anastomotic opening measured three millimeters in diameter, and was protected by a fold of duodenal mucosa. The common duct was sectioned distal to the anastomosis one month after choledochoduodenostomy was performed.

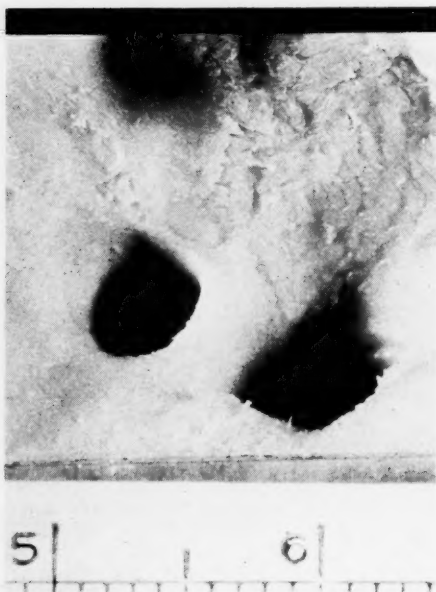


FIG. 7.—A photograph of a double choledochoduodenostomy, from the duodenal side, nine months after operation. The anastomosis on the left was performed after deperitonealization of the duct, and measured three millimeters in diameter, while on the right the duct remained peritonealized, and the opening measured five millimeters in diameter.

cultures. This suggests that anastomotic openings between the bile ducts and gastro-intestinal tract results in the presence of bacteria in the bile.

#### CONCLUSIONS

(1) In the anastomosis of the bile ducts to the gastro-intestinal tract the size of the anastomosis appears to be important.

The necrosing suture must include a bite of tissue about two times the diameter of the normal duct, which results in an opening slightly larger than the diameter of the duct. This results in a lack of stenosis of the stoma which is, on the other hand, small enough to prevent regurgitation of gross contents of the gastro-intestinal tract. If the necrosing suture is made to produce an opening two or three times the diam-



A



B



Fig. 8.—(A) Photograph of fresh specimen of liver, bile ducts, duodenum and anastomosis, five months after operation. (B) Photograph of magnification of the fresh specimen showing the anastomotic opening, which was oval, and measured three millimeters in diameter.



A



B

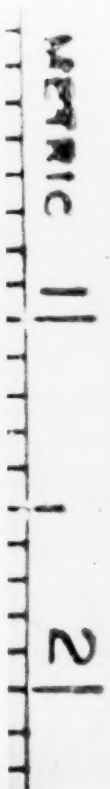


Fig. 9.—(A) Photograph of fresh specimen, nine months after operation, in which cholecystoduodenostomy was performed, and the common duct remained in continuity with the duodenum. (B) Photograph of magnification of the common duct, after fixing in formalin, which measured three millimeters in diameter.

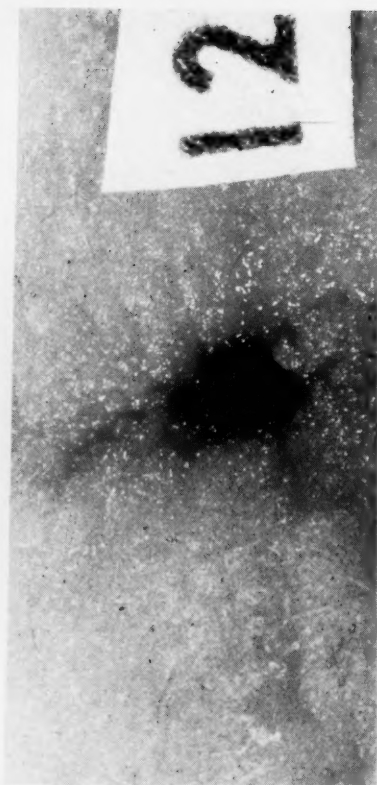
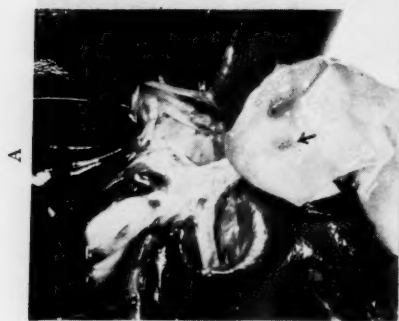


FIG. 10.—(A) Photograph of fresh specimen of liver, gallbladder and stomach wall, with anastomosis performed after operation. (B) Photograph of anastomosis, after fixing in formalin, which measured four millimeters in diameter.

FIG. 11.—(A) Photograph of liver, gallbladder, bile ducts and duodenal wall, with anastomosis performed after division in the duodenal wall, after four months. (B) Photograph of anastomosis, after four months, which measured four millimeters in diameter.

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eter of the normal duct, regurgitation of gross particles of gastro-intestinal contents is common, and dilatation of the ducts, and infection of the liver occurs.

(2) This method of transfixion necrosing suture appears to be a simple procedure to attain this objective, and is more controllable than a direct layer-suture.

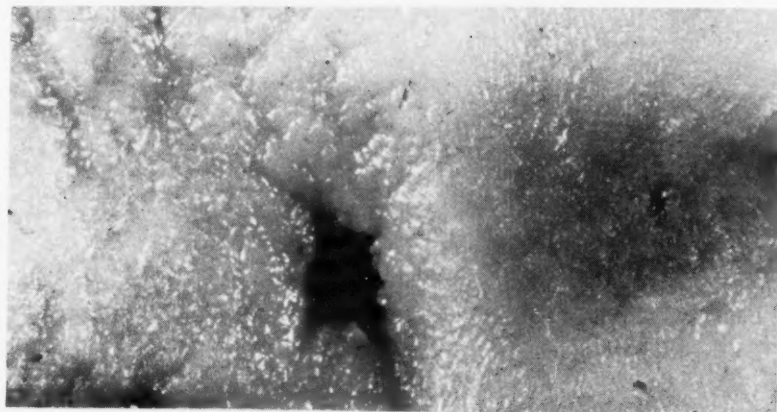
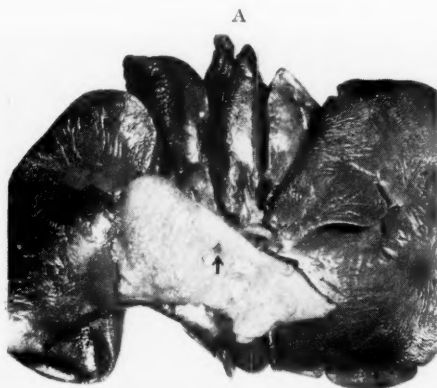


FIG. 12.—(A) Photograph of fresh specimen of liver, common bile duct and duodenal wall, with the anastomosis, shown five months after operation. (B) Photograph of anastomosis, after fixing in formalin, which measured 3 x 5 Mm.

(3) As a transfixion suture a single silk ligature is the best material, and it should always be employed on peritonealized duct, which insures proper adherence of the peritoneal surfaces of the duct and the gastro-intestinal tract.

(4) A silk transfixion necrosing suture for anastomosis between the bile ducts and the gastro-intestinal tract was efficient in 38 anastomoses in 34

FIG. 11.—(A) Photograph of liver, gallbladder, bile ducts and duodenal wall, with anastomosis, prepared by making a longitudinal incision in the duodenal wall, after four months. (B) Photograph of anastomosis, after fixing in formalin, which measured four millimeters, and was point of anastomosis, after four months.

FIG. 10.—(A) Photograph of fresh specimen of liver, gallbladder and stomach wall, with anastomosis, three months after operation. (B) Photograph of anastomosis, after fixing in formalin, which measured four millimeters in diameter.



dogs. It failed in three, where the duct was deperitonealized. In other words, it is a reliable method to produce a controlled size of anastomosis. Its adoption on experimental findings is debatable, but it is an easily performed anastomosis between the bile ducts and the gastro-intestinal tract, and facilitates the operation where the layer-suture procedure is very difficult to perform.

(5) No conclusion could be reached about the most desirable site in the gastro-intestinal tract for anastomosis, except that lack of tension is very important—longitudinal incision through the serosa and the muscle of the gastro-intestinal tract seems desirable.

(6) A silk transfixion necrosing suture requires from two to four days to cut through, and, if carried out in the presence of complete obstructive jaundice, external biliary drainage should be temporarily beneficial.

Assistance in illustrations was rendered by G. W. Reis, M. W. Praddock, and the Photography Department of Rush Medical College.

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DISCUSSION.—DR. WALTMAN WALTERS (Rochester, Minn.): Doctors Brackin and David have applied this method of transfixion suture necrosis anastomosis to the technic of anastomosis between the common bile duct or gallbladder and the duodenum or the stomach, which Doctor Coffey was first to describe in the anastomosis of the ureter to the intestine.

Two years ago, Doctor Brackin presented his experimental studies on ureterosigmoidal anastomosis, and emphasized at that time, as he did again to-day, the fact that when the peritoneum was allowed to remain in contact with the ureter (and in contact with the common bile duct in the experiments of this year), a more satisfactory anastomosis occurred, without the degree of contraction which otherwise resulted when the peritoneum was deflected.

It seems to me that, as Doctor Brackin brought out in his concluding statement, a sufficient period will have to elapse after application of this principle to biliary-intestinal anastomosis for patients, before one can arrive at a definite decision that it is superior to the direct method of anastomosis which we all know.

I am very much interested in Doctor Brackin's report of his results in three cases in which the method had been employed in ureterosigmoidal transplantation. One of these patients now has lived more than 24 months, and has been without evidence of obstruction at the anastomosis, or without evidence of renal infection.

I think the experiments have been well conceived and well carried out. I am not convinced that the method is a superior one in the matter of reduction in the amount of infection in the biliary tract subsequent to its use, in comparison to those cases in which direct anastomosis is used. Furthermore, I never have been thoroughly convinced that a method which is dependent on factors over which the surgeon does not have complete control—and by that I mean transfixion suture necrosis anastomosis—is superior to the direct method of anastomosis.

I should like, also, to call attention to the fact that with the deeply jaundiced patient, where this method of anastomosis is used, in that period of danger, namely, the 48 hours subsequent to operation, in which bleeding is likely to occur and hepatic and renal insufficiency may take place, the great safeguard against those possibilities of bleeding and of the development of hepatic insufficiency immediately after operation is immediate relief of the obstruction. I am sure it has been the experience of all surgeons in operations upon deeply jaundiced patients, that those who fail to recover usually are those whose obstruction has not been completely relieved, and whereas the patient may not have had evidence of bleeding or hepatic or renal insufficiency prior to operation, it may develop immediately subsequent to operation.

Furthermore, I am not convinced that anastomosis of the gallbladder to the stomach or duodenum may not have superior advantages when it is done for the human being over those of anastomosis of common bile duct, remembering, of course, that mention was made of the application of this method to anastomosis of the gallbladder as well as the common bile duct.

In such cases, it seems worthy of emphasis that among human beings, when direct anastomosis of the gallbladder is made to the stomach or duodenum, contrary to these experimental results, a larger anastomosis is preferable to a smaller one, the reason probably being that in the smaller anastomosis edema occurs at the site of the anastomosis, interfering with relief of the obstruction, with bleeding and hepatic insufficiency possibly occurring subsequently.

I think the method is worthy of trial in suitable cases, and I think that it may demonstrate some advantages over the direct method. I should like to suggest to Doctor Brackin that further study might be worth while in determining the relative relationship between intragastric or intraduodenal pressure and intrabiliary pressure among human beings in comparison to such pressures in experimental animals.

I believe the reason that intrahepatic infection develops among so few patients subsequent to cholecysto-enterostomy is that the liver has sufficient natural capacity to withstand infection which undoubtedly occurs, in contrast to the situation in the experimental animal, but in addition, I believe there is a possibility that when complete obstruction is present in the human being the amount of secretory pressure in the biliary tract is sufficient to prevent the fluid in the stomach or duodenum from regurgitating into the extrahepatic biliary tree, even though some of it might reach the gallbladder. In the case of the gallbladder, as was brought out this afternoon, there probably is associated some mechanism

concerned with the emptying or filling of the gallbladder around the valves of Heister, which might exert a protective influence when foreign fluids enter the gallbladder.

DR. THOMAS H. LANMAN (Boston): I was very much interested in hearing the two last speakers. I want to speak of some experiences we have had at the Boston Children's Hospital in treating congenital anomalies of the bile ducts.

We agree with Doctor Walters, that direct anastomosis seems to serve better than any other method, and we are not at all afraid of having a large stoma in these small patients. The results, as we have followed them for eight or ten years, are most satisfactory, and we have been impressed not only with the relief of symptoms but with the very great power of liver regeneration that these young patients exhibit, once the obstructive jaundice is relieved. These patients are usually operated upon at one to two months of age. All of them have had no communication between the liver and gastrointestinal tract. We feel that the direct anastomosis is, if possible, more satisfactory in this type of young patient.

DR. VERNON C. DAVID (Chicago, Ill., closing): I agree with Doctors Walters and Lanman, that in most obstructions, where the gallbladder is still present, the direct anastomosis, by suture of the gallbladder into the gastro-intestinal tract, is a very satisfactory and proper means of anastomosis. My particular interest in this method was stimulated by the difficult cases, where the gallbladder has been taken out, where the ducts are difficult to find, and where the mechanical problem of making a layer of anastomosis between the common duct and the gastro-intestinal tract presents a real problem.

One such instance I should like to relate briefly, where the principle of necrosing suture was employed. A patient, operated upon elsewhere for gallstones, had, following her operation, a rapidly deepening jaundice; she was told by her surgeon that an anomaly of the ducts had been present, so that it was necessary to insert a tube in part of the ductile system to convey the bile. The jaundice persisted, and was accompanied by the usual picture of sepsis, chills, and fever.

Two years after this occurrence, the patient being deeply jaundiced, coming to this country, we explored her and found that a red rubber tube had taken the place of part of the common duct and lay in scar tissue very close to the liver. After removal of this tube, the only portion of the duct that I was able to find, was an opening in the liver on the same plane as the liver, and the distal end of the common duct we were not able to identify.

Under these conditions, we attempted to repair by the use of the transfixion, necrosing silk suture introduced through the duodenum, on the basis that while we knew we would have bile leakage around the anastomosis, the approximation of the peritoneum of the liver and the duodenum would agglutinate, to some degree, these two organs, so that, as the necrosing suture cut through, the bile drainage could be reestablished through the hepatic duct into the duodenum. Therefore, the duodenum was sutured posteriorly to the hepatic duct on Glisson's capsule and a necrosing suture was put through the duodenal wall, then the duodenum sutured anterior to the duct. This patient drained bile four or five days, and then began to show bile in the intestinal tract, and has had normal bile drainage since. It is too short a period to say how permanent this new anastomosis will be, and how little fraught with danger it may be, but at any rate, here the principle was used, to our great satisfaction, in creating a new stoma, the size of which could be controlled fairly accurately by the necrosing suture in the duodenum.

It seems to me that it is in these cases that the method is useful, and it appeals to me because it allows the surgeon to predicate, fairly accurately, the size of the anastomosis as well as to greatly simplify the technic where the going is difficult.

## ASEPTIC, IMMEDIATE ANASTOMOSIS FOLLOWING RESECTION OF THE COLON FOR CARCINOMA \*

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THE HISTORY of the surgical treatment of cancer of the colon parallels the history of surgical progress in overcoming the hazards of infection. The general principles for the treatment of malignancy anywhere apply in cancer of the colon. The primary tumor must be widely excised in one block with the tributary lymphatic channels and nodes, but in cancer of the colon this surgical procedure must be carried out upon an organ the lumen of which is teeming with bacteria. Peritonitis was, and still is, one of the chief causes of mortality following operation. The early operations upon cancer of the colon were performed in the era of antiseptic surgery and the mortality was very high. In other fields of surgery, the hazards of infection declined with the development of asepsis, but in operations upon the colon, it has been far more difficult to solve the problem of avoiding contamination of the peritoneal cavity, and of the wound in the abdominal wall. DeBovis,<sup>5</sup> in 1900, and more recently Rankin<sup>36</sup> and Cope,<sup>7</sup> have published excellent histories of the early surgical procedures employed in carcinoma of the colon. We shall only mention a few points of interest in the more recent developments.

At an early date, surgeons began to concern themselves with developing methods for removing the malignant lesion and at the same time avoiding fatal infections. Thomas Bryant,<sup>3</sup> in 1882, was the first surgeon to report the successful removal of a carcinoma of the colon by pulling the growth outside the abdominal wall and suturing the limbs of the bowel to the abdominal incision, thus avoiding contamination of the peritoneal cavity. Barton,<sup>2</sup> of Philadelphia, in 1888, also reported the successful removal of a carcinoma of the colon by an extra-abdominal resection. The growth which was at the ileocecal valve was withdrawn from the abdomen, cut off, and an enterotome was immediately applied to crush the spur between the ileum and the ascending colon. The abdominal wound was closed around the limbs of the bowel which was brought out of the abdomen. Bloch,<sup>4</sup> of Copenhagen, also reported a successful result by this method in 1892. Paul,<sup>29</sup> in 1895, published his classic article describing his experience with seven patients, which, he said: "... represents the education of an individual surgeon." His technic changed from one of immediate anastomosis to the safer procedure of freeing the growth sufficiently to draw it outside the abdomen. The descending and ascending limbs of the bowel attached to the tumor were sutured together, the growth and the adjacent portions of the bowel were cut

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off, and glass tubes tied into the projecting limbs of the colon (Fig. 1). The spur was later crushed with a Dupuytren's clamp, and still later the colostomy was closed by a plastic procedure, without entering the peritoneal cavity. A somewhat similar procedure was adopted by Mikulicz.<sup>23</sup> However, he did not suture together the limbs of the bowel protruding from the abdomen. In

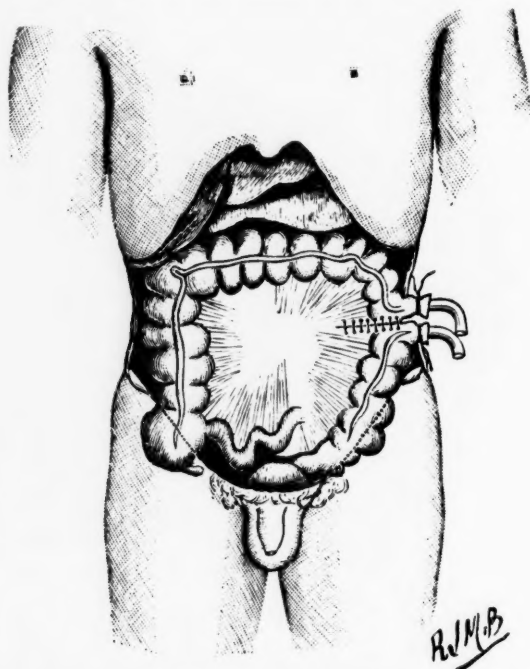


FIG. 1.—Reproduction of the illustration from Paul, showing the technic used. (Liverpool Med. Chir. Jour., 1895.)

1903, he<sup>23</sup> reported 24 operations by this method, with four deaths. This mortality of 17 per cent contrasts very favorably with the 30 to 50 per cent mortality associated with immediate anastomosis of the bowel at that time.

The principle of exteriorization was then adopted generally by American surgeons, who continued to practice it, under the name of the "Mikulicz procedure" for the next 20 years. Both Mikulicz, in 1903, and Paul,<sup>30</sup> in his later and final article in 1912, referred to the importance of removing an adequate portion of the mesentery adjacent to the growth. Paul, and Mikulicz at the time of his report, practiced immediate removal of the growth at the time of operation. However, these two procedures, the immediate removal of the growth and the excision of the lymphatics and adjacent mesentery, were generally neglected by American surgeons. In one large series<sup>34</sup> of cases the incidence of recurrence of carcinoma in the wound was as high as 12 per cent. The mortality of the procedure, while lower than that of immediate anastomosis, was still far from satisfactory. Miller,<sup>24</sup> in 1923, reported a series of 70 patients with carcinoma of the colon, treated in the Johns Hopkins Hospital from 1889 to 1919, operated upon by either

the exteriorization or open anastomosis methods. The mortality of the series was 35 per cent. Nordmann,<sup>26</sup> in 1926, reported an approximately equal mortality with resection and immediate anastomosis and the exteriorization methods. Two hundred and eighty-eight cases were operated upon by the first method with a 29 per cent mortality, while 144 patients were operated upon by the exteriorization technic with a 28 per cent mortality.

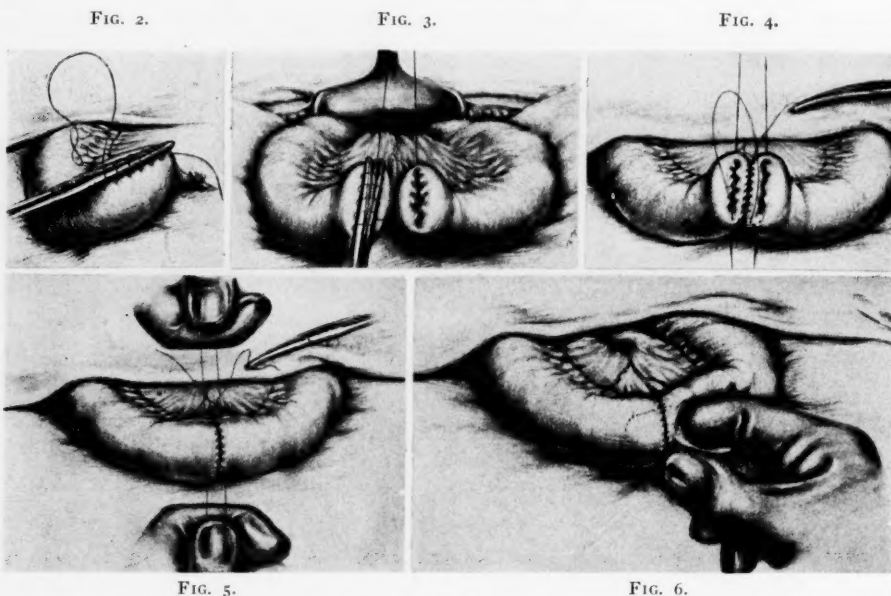
During the next decade, there was a growing dissatisfaction with this method. Sistrunk,<sup>40</sup> in 1928, pointed out the limitations of the procedure. In 1930, Rankin<sup>34</sup> returned to old principles in the exteriorization operation by advocating immediate removal of the tumor and wide excision of the mesentery. Clamps were left on the protruding ends of the bowel for a few days. The growing dislike of the delayed extra-abdominal anastomosis was again expressed by Cheever,<sup>6</sup> in 1931, when he advised immediate anastomosis after resection of the bowel. He reported an operability of 55 per cent in patients operated upon at the Peter Bent Brigham Hospital since 1913, with the relatively low operative mortality of 18 per cent. In the decade between 1930 and 1940, Lahey,<sup>17</sup> and Rankin<sup>34</sup> are the outstanding advocates of extra-abdominal resection and delayed anastomosis of the colon. The former<sup>16</sup> even applies the procedure to growths in the right half of the colon, while Rankin<sup>35</sup> prefers a primary anastomosis of the ileum and colon by an aseptic method. Both these authors have had a low operative mortality with the exteriorization operation.

Other surgeons have not been so successful. Joll,<sup>13</sup> in 1938, expressed some very decided objections to the exteriorization operation, and states his preference for immediate anastomosis. Finsterer,<sup>8</sup> in 1939, shared these views. He employed immediate anastomosis whenever possible and reported an operability of 80 per cent with an operative mortality of 17 per cent. Mayo and Simpson,<sup>21</sup> in the same year, reported 95 cases of exteriorization in carcinoma of the transverse colon, with an operative mortality of 20 per cent, and contrasted this with resection and primary anastomosis in 36 cases with an 11 per cent mortality.

When the older cases are included in reported series, the operative mortality remains high. Grinnel,<sup>12</sup> in 1939, reported a 27 per cent mortality in patients with carcinoma of the colon from 1916 to 1932. Ransom,<sup>38</sup> from Ann Arbor, in the same year, reported an operative mortality of 30 per cent in cases of carcinoma of the right side of the colon from 1925 to 1937. In the more recent series the mortality is lower. Naffziger and Bell,<sup>25</sup> in 1940, reported an 11 per cent mortality from 1930 to 1940. These last three reports included cases of open anastomosis as well as exteriorization procedures. Finally, Patterson and Webb,<sup>28</sup> in 1940, reported 70 resections of the large bowel for carcinoma, all by the exteriorization method. There were 19 deaths in 70 cases. The authors excluded seven of these deaths for various reasons. If these seven deaths are included, the operative mortality in their series is 27 per cent. Thus, it appears that the exteriorization procedure in the hands of the general surgeon still carries a high mortality.



Owing to the discomfort and the prolonged convalescence of the exteriorization method, other means of avoiding the ever constant danger of infection have been sought. Kerr<sup>15</sup> has recently reviewed the various methods which have been proposed for anastomosing the bowel without opening its lumen. Prior to 1908, some 25 of 200 methods of intestinal anastomosis were designed to accomplish an aseptic anastomosis. Since 1908, 21 additional



FIGS. 2 to 6, inclusive.—Reproductions from Kerr, showing the various steps in the aseptic end-to-end anastomosis by the basting-stitch method. (J.A.M.A., 1923.)

methods have been proposed. All of them are variations of the fundamental procedure of temporarily closing the cut ends of the bowel by clamps, sutures, or ligatures, uniting the bowel by suture over the temporary occluding device, and then withdrawing the clamp or suture. Only a few of the many devices or methods will be discussed here, *i.e.*, those which have proved their worth in clinical practice.

Schoemaker,<sup>39</sup> in 1921, was the first to report the extensive use of an aseptic method of anastomosis of the large bowel in patients. He divided the serous and muscular coats of the bowel and then applied fine clamps to the mucosa. He cut between the clamps with a cautery and made his anastomosis with interrupted sutures, finally withdrawing the clamps. He says of the procedure: "During the whole operation, the lumen of the colon has not been opened, and we have not seen or touched the inner side of the mucosa." He performed this operation 40 times for cancer of the colon, with three deaths, an operative mortality of 8 per cent. Probably due to the stimulus of these excellent results, the decade of 1920 to 1930 was characterized by an increasing interest in the aseptic method of immediate anastomosis. In 1923, Kerr<sup>14</sup> gave an excellent description of the clinical use of the basting-

stitch method (Figs. 2 to 6, inclusive) which he and Parker<sup>27</sup> had described 15 years before. In 1924, Pringle<sup>31</sup> modified Schoemaker's method of anastomosis over clamps, by omitting the division of the seromuscular coats of the bowel. Following these descriptions of various aseptic technics, more surgeons began to apply the method clinically in carcinoma of the colon. Gibbon,<sup>11</sup> in 1932, reported 15 cases of cancer of the colon resected by the Kerr basting-stitch method, with three deaths, a mortality of 20 per cent.

During the past seven years, a number of reports have appeared contrasting the use of the aseptic method with exteriorization and open anastomosis. All of these statistical studies show a lower mortality with the aseptic technic. Wilkie,<sup>44</sup> in 1934, reported a series of cases some of which were done by the exteriorization method and some by an aseptic technic over clamps. The mortality was lower with the latter procedure. In 1937, MacFee<sup>20</sup> reported a large series of cases from St. Luke's and the New York Hospitals, the former since 1922, and the latter since 1929. He showed a definitely lower mortality with the aseptic technic. In 1939, Stone and McLanahan<sup>42</sup> reported a large series of cases operated upon by both the aseptic and open methods of anastomosis. There was a considerably lower mortality when the aseptic method was employed. In the same year, Allen<sup>1</sup> discussed a large series of cases of carcinoma of the colon occurring at the Massachusetts General Hospital. The operability was 58 per cent, and the operative mortality 24 per cent. He expressed a strong preference for the aseptic Parker-Kerr anastomosis, preceded by colostomy or cecostomy; and in the sigmoid colon, he reported an operative mortality of 14 per cent by aseptic methods and 23 and 21 per cent by the open and exteriorization methods, respectively. In 1939, Wilkie<sup>45</sup> contrasted the exteriorization and aseptic technics in a larger series of his own patients and again found a lower mortality with the latter procedure.

Aside from contamination occurring at the time of operation which the aseptic methods attempt to avoid, there is always the danger of late peritonitis five or ten days after the operation from necrosis or leakage at the suture line. This danger is perhaps easily as great as that of immediate contamination during the operation, and has been responsible for the continuation of the use of exteriorization in the presence of adequate aseptic methods of anastomosis. Because of this constantly recurring danger, lateral anastomosis was early proposed as a safer procedure than end-to-end union of the large bowel, in the belief that there would be fewer instances of leakage from the suture line. The anastomosis is made along the antimesenteric border of the bowel without interrupting the blood supply to the wall of the colon. With the end-to-end anastomosis however, if the bowel is divided at right angles to its long axis, there is danger of necrosis along the antimesenteric portion of the suture line because of the vertical direction of the small terminal arteries supplying the wall of the intestine. These arteries may be crushed by the clamp or included in a ligature, thus interfering with the blood supply of the antimesenteric border of the bowel.

In 1917, Lockhart-Mummery<sup>18</sup> published a classic report on the advantage of end-to-end, as opposed to side-to-side, anastomosis. He pointed out the dangers of leakage from bowel contents being driven by peristaltic action against closed ends of the bowel with the lateral anastomosis. He believed that the failures with end-to-end anastomosis in the past were due to improper attention to the terminal blood vessels of the colon which pass around the bowel wall at right angles to its long axis. He, consequently, advised cutting the bowel at an angle, so that a greater portion of the antimesenteric border was removed, thus insuring an adequate blood supply to the cut margins of the bowel. Kerr<sup>14</sup> in 1923, again urged the advantages of end-to-end anastomosis. Meillère,<sup>22</sup> in 1927, published an excellent account of the blood supply of the wall of the colon, and its surgical applications. He injected the vessels supplying the normal colon and studied the relation of the terminal arteries to the appendices epiploicae. The injections were then repeated after various ligations of the arteries. He confirmed Lockhart-Mummery's opinion that it was best to divide the colon obliquely, removing more of the antimesenteric than of the mesenteric border of the bowel, thus insuring an adequate blood supply to the cut ends of the bowel. He believed that it was safe to remove the fat for a short distance from the cut ends of the colon before suturing, but recommended exercising great care in removing the appendices epiploicae, as the straight terminal arteries supplying the wall of the colon run in the base of these appendices. Stewart and Rankin,<sup>41</sup> in 1933, also published an excellent study of the blood supply to the walls of the colon. A correct appreciation of the blood supply to the colon should obviate the danger of necrosis at the suture line in end-to-end anastomosis.

It has not been borne out in reported series of cases, that the mortality of the side-to-side anastomosis is lower. Miller,<sup>24</sup> in 1923, reviewing cases of carcinoma of the colon at Johns Hopkins Hospital, found a higher mortality with lateral, as opposed to end-to-end anastomosis. Raiford,<sup>32</sup> in 1933, advised lateral anastomosis in resection of the transverse colon. However, two years later, in reviewing a large series of cases of cancer of the colon, he<sup>33</sup> found the operative mortality almost three times higher with lateral anastomosis as compared with end-to-end union.

The recent wide adoption of chemotherapy for the control and treatment of infection will undoubtedly lower the mortality of resection of the colon for cancer. Garlock and Seley<sup>10</sup> were the first to report the use of sulfanilamide in resections of the colon. In a series of cases, they made cultures from the serous surface of the colon, from the muscular walls and from the surface of malignant growths. They found the predominating organism to be the hemolytic streptococcus. On the basis of this study, they administered sulfanilamide orally prior to and following operations on the colon. In this group of patients, at the time of operation, the same type of cultures were repeated and hemolytic streptococci were found to be absent in all instances. They reported nine resections of the colon for carcinoma, with one death.

# ASEPTIC ANASTOMOSIS

This fatality was not due to peritonitis. In the following year, Lockwood and Ravdin<sup>19</sup> reported using sulfanilamide preceding and following 11 resections of the colon for carcinoma. There was one death from coronary thrombosis. Firor,<sup>9</sup> in December, 1940, was the first to report on the use of sulfanilylguanidine in colonic surgery. The drug was administered for about one week preceding operation in a series of patients which included some very difficult resections and anastomoses of the large bowel. There were no fatalities and no instances of peritonitis, in spite of gross contamination and soiling in a number of cases.

The present report is based upon a series of 120 patients with carcinoma of the colon proximal to the rectosigmoid. It comprises all patients with carcinoma of the colon admitted to the Pennsylvania and the Bryn Mawr Hospitals from 1928 to 1941. Nine of these patients refused operation, or died shortly after admission, without being operated upon. In 52 patients, the growth was found to be inoperable, but 59 of the remaining 111 patients underwent radical resection of the colon, an operability of 53 per cent. There were 15 deaths in the hospital following operation, an operative mortality of 25 per cent. The operations were performed by 20 different surgeons (Table I). Five surgeons operated upon 80 of the patients; the remaining 31 patients were operated upon by 15 surgeons. As can be seen in Table I, the more experienced surgeons had operability rates varying between 50 to 83 per cent. The other 15 surgeons had the very low operability rate of 29 per cent. The operative mortality of the five experienced surgeons varied between zero and 37 per cent, the higher mortalities being associated, in general, with higher rates of operability.

TABLE I  
RECORD OF INDIVIDUAL SURGEONS

Surgeon	Number of Patients Operated Upon	Number of Patients from Whom Tumor Was Removed	Operability Per Cent	Deaths in Hospital Where Tumor Was Removed	Hospital Mortality Where Tumor Was Removed. Per Cent
A	22	15	68	5	33
B	20	10	50	2	20
C	14	7	50	0	0
D	12	10	83	3	30
E	12	8	67	3	37
15 surgeons	31	9	29	2	22
Totals, 20 surgeons	111	59	53	15	25

When the resections are grouped according to the type of operation performed, it can be seen that the aseptic anastomosis has the lowest operative mortality, 13 per cent (Table II). The aseptic anastomoses were performed by the Kerr basting-stitch method in all these patients. Exteriorization is next in order with 29 per cent, whereas the open anastomoses had an operative mortality of 38 per cent. Conversely, the number of patients alive and

without evidence of metastasis is higher in the group with aseptic anastomosis, and smallest in the group with the open anastomosis.

All five of the more experienced surgeons employed more than one type of operation upon their patients. The results obtained by these five surgeons can be seen in Table III. The operative mortality again was lowest with

TABLE II  
CASES IN WHICH TUMOR WAS REMOVED

Type of Operation	Number of Patients	Deaths in Hospital		Living Without Metastasis	
		Number	Per Cent	Number	Per Cent
Aseptic anastomosis	24	3	13	9	38
Exteriorization	14	4	29	4	29
Open anastomosis	21	8	38	4	19
Totals	59	15	25	17	29

TABLE III  
MORTALITY WITH DIFFERENT TECHNIQUES OF SURGEONS A, B, C, D AND E

	Aseptic Anastomosis	Exteriorization	Open Anastomosis
Patients	20	11	19
Deaths in hospital	3	3	7
Mortality, per cent	15	27	37

the aseptic anastomosis, 15 per cent; next with exteriorization, 27 per cent; and very high with open anastomosis, 37 per cent. The wound complications (Table IV) were more frequent with open anastomosis than with the other

TABLE IV

WOUND COMPLICATIONS

Type of Operation	Wound Infections		Abscess or Local Peritonitis		General Peritonitis		Evisceration		No Complication	
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Aseptic anastomosis	5	21%	2	8%	2	8%	1	4%	14	58%
Exteriorization	2	14%	0	0%	3	21%	0	0%	9	64%
Open anastomosis	5	24%	4	19%	3	14%	0	0%	9	43%

two types, in which the incidence was approximately the same. General peritonitis occurred more frequently following the open anastomosis and exteriorization than it did with the aseptic methods.

In Table V, the type of operation performed in different regions of the colon is shown. In the right colon, ten resections were performed by the aseptic technic with no deaths, while with the open anastomosis there were three deaths in ten cases. There were only two resections of the transverse colon, and both were without mortality. There was little difference in the mortality of the three methods in the splenic flexure and descending colon. In the sigmoid colon, there was little difference between the aseptic and exteriorization methods, whereas the operative mortality with open anastomosis was 80 per cent.

The question as to whether cecostomy or colostomy should be employed



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TABLE V  
TYPE OF OPERATION

Location of Lesion	Aseptic Anastomosis			Exteriorization			Open Anastomosis			Totals		
	Cases	Deaths	Mort. Per Cent	Cases	Deaths	Mort. Per Cent	Cases	Deaths	Mort. Per Cent	Cases	Deaths	Mort. Per Cent
Cecum; ascending colon; hepatic flexure	10	0	0%	1	0	0%	10	3	30%	21	3	14%
Transverse colon	1	0	0%	0	0	0%	1	0	0%	2	0	0%
Splenic flexure and descending colon	4	1	25%	3	1	33%	5	1	20%	12	3	25%
Sigmoid colon	9	2	22%	10	3	30%	5	4	80%	24	9	38%

preceding a direct attack on the tumor has been discussed for many years. It is generally agreed, at present, that if any degree of obstruction exists, a preliminary decompression should be undertaken. It is also agreed that a certain number of cases do not require such a preliminary operation. However, it is probably always safer, even in the patients without obstruction, to perform a cecostomy at the time of operation, when a primary anastomosis of the left colon is performed.<sup>37</sup> Table VI contrasts the mortality in the cases without decompression, with the mortality in cases in which the bowel was decompressed, either previously, or at the time that the tumor was removed. With the aseptic technic there was no difference in the operative mortality, although twice as many cases were performed without any decompression. With exteriorization and open anastomosis, the mortality was much higher in the cases without decompression of the bowel.

TABLE VI  
CECOSTOMY AND COLOSTOMY

Type of Operation	Decompression of the Bowel Before, or at Time of Operation			No Decompression of the Bowel		
	Number of Patients	Deaths in Hospital	Operative Mortality Per Cent	Number of Patients	Deaths in Hospital	Operative Mortality Per Cent
Aseptic anastomosis	8	1	13%	16	2	13%
Exteriorization	9	2	22%	5	2	40%
Open anastomosis	12	3	25%	9	5	56%
Totals	29	6	21%	30	9	30%

Appended are brief histories of the 15 patients who died following operation.

## ABBREVIATED CASE REPORTS

**Case 1.**—Female, age 50, with carcinoma of descending colon. August 1, 1928, resection, with open end-to-end anastomosis. Had febrile postoperative course. Numerous stools per rectum on third, fourth, and fifth postoperative days. On sixth postoperative day, pain in upper left quadrant of abdomen accompanied by tenderness and generalized abdominal distention. Pulse rate and temperature both rose. Signs of circulatory collapse developed seven hours later, and patient died eight hours after onset of pain, presumably from peritonitis and gross leakage at the suture line. No postmortem.

**Case 2.**—Male, age 35, with carcinoma of the sigmoid. September 19, 1928, the growth in the sigmoid, together with the left half of the colon was resected, and an open anastomosis was performed between the midsigmoid and the midtransverse colons. The proximal bowel was distended. No cecostomy was made. The temperature was elevated from the first postoperative day. He died six days after operation with signs and symptoms of peritonitis. No postmortem.

**Case 3.**—Male, age 75, with carcinoma of the sigmoid. October 22, 1928, entire left colon resected because of involvement of the transverse colon in the malignancy. Open anastomosis performed between the transverse and sigmoid colons, with some contamination. A colostomy with mushroom catheter was made just proximal to the site of the anastomosis. The patient developed pyelonephritis and uremia. He had to be catheterized throughout the postoperative course. Death occurred on the fourteenth postoperative day, presumably from renal failure. There was no evidence of peritonitis at any time. No postmortem.

**Case 4.**—Male, age 61, with carcinoma of the sigmoid. November 16, 1928, sigmoid resected and end-to-end aseptic anastomosis made by Kerr basting-stitch method. Two continuous sutures of catgut were used to make the anastomosis. There was no obstruction, and no cecostomy was performed. There were no bowel movements following operation. On the sixth postoperative day, there was evidence of peritonitis. The patient was operated upon; generalized peritonitis found; and the abdomen drained. The patient died on the seventh postoperative day.

**Case 5.**—Male, age 58, with carcinoma of the sigmoid. November 5, 1930, the sigmoid was resected, and an open anastomosis performed. Death occurred two days later with signs and symptoms of generalized peritonitis. No postmortem.

**Case 6.**—Female, age 55, with carcinoma of the descending colon. November 13, 1930, a loop-colostomy of the transverse colon was made because of obstruction. No spur was formed. The colostomy was not opened for 11 days. Two months later, an open side-to-side ileosigmoidostomy was performed. Two months later still, the descending colon, with the growth was removed and the ends of the colon inverted. Death occurred one month later. Postmortem examination revealed that the blind end of the colon at the splenic flexure had opened. There was a sinus tract extending down to the left lower quadrant of the abdomen, with extensive ramifications in the abdominal wall.

**Case 7.**—Female, age 66, with carcinoma of the descending colon. September 8, 1931, the first stage of an exteriorization operation was performed. The growth was withdrawn from the abdomen and the limbs of the colon were sutured together and to the parietal peritoneum. Three days later the bowel containing the growth was removed. Death occurred on the same day with signs and symptoms of peritonitis. There had been a gradually increasing temperature and pulse rate and marked distention since initial operation. No postmortem.

**Case 8.**—Female, age 80, with carcinoma of the descending colon. April 26, 1933, cecostomy was performed because of an obstruction. Twenty-two days later the descending colon with the growth was resected by the Kerr basting-stitch method. Some contamination occurred when the ends of the colon were inverted by the basting-stitch. Death occurred four days later with signs and symptoms of peritonitis. No postmortem.

**Case 9.**—Female, age 53, with carcinoma of the ascending colon. August 22, 1934, the right half of the colon was resected and an open side-to-side anastomosis made between the ileum and the transverse colon. The patient died on the seventh postoperative day, with signs and symptoms of generalized peritonitis. No postmortem.

**Case 10.**—Male, age 79, with carcinoma of the sigmoid. May 29, 1935, the growth was exteriorized. The patient died three days later, with signs and symptoms of generalized peritonitis. No postmortem.

**Case 11.**—Male, age 63, with carcinoma of the sigmoid. December 18, 1935, the growth was resected and a primary anastomosis performed by the Kerr basting-stitch method. Cecostomy was performed at the time of operation. The patient had no bowel

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movements by rectum for 11 days following the operation. After this he had normal stools. Twenty-one days after operation the patient died, with signs and symptoms of bronchopneumonia, probably secondary to congestive failure, as there were râles throughout his lungs for ten days before death. No postmortem.

**Case 12.**—Female, age 54, with carcinoma of the hepatic flexure. September 26, 1936, an open side-to-side ileosigmoidostomy was performed because of obstruction. Twenty-four days later the right colon was resected, and the blind ends of the transverse colon and the terminal ileum inverted. Five days after operation the patient died, with signs and symptoms of general peritonitis. At autopsy, the peritonitis was found to be due to leakage from the end of the blind stump of the transverse colon.

**Case 13.**—Male, age 69, with carcinoma of the sigmoid and partial obstruction for eight days. July 7, 1939, the growth was withdrawn from the abdomen through a right lower rectus sheath incision. The limbs of the bowel were sutured together and to the parietal peritoneum. The mesentery was not excised. Three days after operation, the proximal loop of the colon was opened and a catheter inserted. Death occurred the following day, four days after operation, following a gradual rise in temperature and pulse rate. Death was probably due to peritonitis, the infection originating from the sutures introduced into the distended proximal loop of bowel. No postmortem.

**Case 14.**—Male, age 53, with carcinoma of the sigmoid. November 29, 1937, the growth was exteriorized. He developed a wound infection and died on the twelfth post-operative day.

**Case 15.**—Male, age 69, with carcinoma of the ascending colon. May 4, 1939, the right half of the colon was resected and an open anastomosis made between the terminal ileum and the transverse colon. There was some contamination of the operative field. The patient developed a wound infection and a localized peritonitis, and later a fistula of the ileum. He ran a progressive downhill course and died ten weeks after operation. No postmortem.

In analyzing these deaths, it is apparent that the mortality is chiefly due to infection. Of the 15 deaths in this series, ten were due to generalized peritonitis, three to wound infections and localized peritonitis, and two to causes probably unrelated to the operation. Of the ten deaths from peritonitis, five followed resection with open anastomosis of the colon. Two of these were of the right side of the colon and three of the left. Generalized peritonitis occurred following the first stage of an exteriorization procedure in three patients. Two of the growths were in the sigmoid and one in the descending colon. Finally, two of the ten deaths due to peritonitis followed an aseptic anastomosis. In one case, a cecostomy to protect the suture line was not performed; in the other case, contamination occurred during the operation from an error in the aseptic technic. There were three deaths from wound infection and localized peritonitis. All three lesions were in the left half of the colon, two following open anastomosis of the bowel and one following the first stage of an exteriorization procedure.

Four reports have appeared contrasting the operative mortality of aseptic anastomosis with the mortality of exteriorization or open anastomosis. These four reports have been summarized in Table VII. Two hundred and forty-six aseptic resections of the colon were performed with an operative mortality of 14 per cent. One hundred and twenty-four exteriorization operations were performed, with a mortality of 27 per cent. Seventy-two open anas-

TABLE VII

OPERATIVE MORTALITY IN RESECTION OF THE COLON FOR CARCINOMA BY AUTHORS USING DIFFERENT METHODS

Author	Number of Patients	Deaths in Hospital	Operative Mortality Per Cent	Type of Operation
MacFee.....	56	9	16%	Aseptic anastomosis
Wilkie.....	95	15	16%	
Stone and McLanahan.....	71	8	11%	
Gibbon and Hodge.....	24	3	13%	
Totals.....	246	35	14%	
MacFee.....	68	19	28%	Exteriorization
Wilkie.....	42	9	21%	
Gibbon and Hodge.....	14	5	36%	
Totals.....	124	33	27%	
MacFee.....	32	6	19%	Open anastomosis
Stone and McLanahan.....	19	5	26%	
Gibbon and Hodge.....	21	8	38%	
Totals.....	72	20	28%	

tomoses were performed, with a mortality of 28 per cent. Thus, in this group of patients the operative mortality with exteriorization or open anastomosis is approximately double the mortality associated with aseptic anastomosis.

The surgical therapy of tumors of the colon, proximal to the rectum and rectosigmoid, involves resection of the bowel with the contained tumor and the reestablishment of the continuity of the gastro-intestinal tract. This surgical procedure is fraught with great danger of infection because the lumen of the colon contains more virulent bacteria than are found in any other portions of the body. The chief problem in the surgical therapy of cancer of the colon is now, and always has been, the avoidance of peritonitis. The means of avoiding such infection may be briefly summarized under four heads:

(1) No type of major operative procedure to remove the growth should be performed in the presence of any degree of obstruction of the colon. The obstruction should always be relieved first by drainage of the colon through a cecostomy<sup>43</sup> or colostomy. When the latter procedure is employed, it should always be performed at a considerable distance proximal to the growth, *i.e.*, in the right half of the transverse colon, in order not to interfere with subsequent operative manipulations involved in the removal of the tumor. In obstruction of the right half of the colon, which cannot be relieved by non-operative means, the fecal current should be diverted by an ileotransverse colostomy.

(2) Contamination of the peritoneum and of the abdominal wound should be avoided at the time of the operative attack on the tumor. This can be done either by exteriorization of the growth with its removal after closing the abdominal incision, or by performing the anastomosis by some form of aseptic technic, in which the lumen of the colon is not opened or entered during the performance of the anastomosis. It is more difficult, and time-consuming, to avoid contamination in an open anastomosis than when an aseptic method is used.

(3) Late peritonitis is almost always the result of leakage from the suture line, or necrosis of the bowel wall where primary anastomosis has been performed. Such a catastrophe is often due to interference with the blood supply to the wall of the colon at the site of the anastomosis, and can be prevented by proper knowledge and technic. In addition, the performance of a cecostomy at the time of the primary anastomosis where the growth involves the left half of the colon will help to avoid distention of the bowel above the anastomosis,<sup>37</sup> which is a factor in producing leakage and peritonitis. The late peritonitis which follows exteriorization procedures is probably due either to infection arising from sutures entering the bowel lumen when the spur is formed, or to necrosis of the bowel as it passes through the abdominal wall from interference with its blood supply. Both these complications can be avoided by suitable technic.

(4) The sulfonamides are of undoubted value in colonic surgery. Sulfanilamide should be used orally and locally at the time of operation, until other compounds have been shown to be superior in controlling accidental contamination.

#### SUMMARY

One hundred and twenty cases of carcinoma of the colon, proximal to the rectosigmoid, have been reviewed. These cases comprise all the patients admitted to the Pennsylvania and the Bryn Mawr Hospitals for this condition from 1928 to 1941. One hundred and eleven of these patients were operated upon, and in 59 the tumor was removed, an operability rate of 53 per cent. The gross mortality of the whole series of patients in which the tumor was removed was 25 per cent.

The purpose of this study is to determine the operative mortality of the three main types of operative procedures: Aseptic immediate anastomosis; extra-abdominal resection, with delayed anastomosis; and immediate anastomosis of the opened bowel. Twenty-four patients were operated upon by the aseptic technic, three of these died in the hospital, giving an operative mortality of 13 per cent. Fourteen patients were operated upon by exteriorization methods, with four deaths in the hospital, an operative mortality of 29 per cent. In 21 patients, an open anastomosis of the bowel was performed, with eight deaths in the hospital, an operative mortality of 38 per cent.

This series of cases is too small to have statistical significance. However, when these statistics are combined with those reported by MacFee, Wilkie, and Stone and McLanahan, the combined percentages are probably of real significance. Two hundred and forty-six patients were operated upon by the aseptic technic, with 35 deaths, an operative mortality of 14 per cent. One hundred and twenty-four patients were operated upon by exteriorization methods, with 33 deaths, an operative mortality of 27 per cent. Finally, 72 patients underwent an open anastomosis of the colon. Twenty of these patients died, an operative mortality of 28 per cent.



These combined statistics appear to indicate that in the hands of the general surgeon aseptic, immediate anastomosis is the operation to be preferred.

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DISCUSSION.—WILLIAM F. MACFEE, M.D. (New York, N. Y.): The surgical removal of carcinoma of the colon, as Doctors Gibbon and Hodge have said, was seldom undertaken in the days of antiseptic surgery. As a matter of fact, celiotomy was not often undertaken for any purpose.

With the establishment of asepsis, abdominal surgery received a great impetus, and there were some who had the hardihood to attempt the removal of cancer of the colon. Apparently, the number was few because, according to Rankin, only ten resections were on record in 1880; seven of these had failed, a mortality of 70 per cent. Rankin states that the number of resections had increased to 48 by 1890, and the mortality had decreased to 45 per cent. Heineke described an exteriorization operation in 1884, but it is probable that all of the resections reported, up to 1890, were done by the open method within the abdomen.

The operation for which Bloch, Paul, and Mikulicz share credit, brought about a substantial reduction in the operative mortality and the exteriorization procedure was widely accepted, but like all other operations it was not without faults, and its universal application was soon questioned.

Reichel, in 1911, contended that the results of primary resection carried out under proper conditions compared favorably with the results of resection preceded by exteri-

zation, and offered statistical proof of his contention. His criteria for primary resection were:

- (1) That the general condition of the patient must be such that a somewhat lengthy operation is permitted.
- (2) The intestine proximal to the tumor must not harbor any considerable accumulation of fecal material.
- (3) The intestine must be viable and free of circulatory disturbances.
- (4) It must be possible to suture the ends of the intestine together without tension.

He also admonished care in placing the sutures, accuracy of approximation, and emphasized exactitude rather than speed of operation. These rules are as sound to-day as when first formulated.

During the 30 years that have passed since Reichel proposed these criteria of safety, the development of relatively aseptic methods of anastomosis has further diminished the risks of end-to-end suture. Doctors Gibbon and Hodge, and others, have shown that, with suitable precautions, aseptic, immediate anastomosis has a lower mortality rate than methods which are commonly presumed to be more conservative. This appears to be true even when the operating is distributed among a considerable number of the Surgical Staff of a General Hospital. It is also a matter of significance that the largest number of patients who were well and free of recurrence in Doctors Gibbon and Hodge's series was in the group with aseptic anastomosis.

Considerably less than one-half of the patients who present themselves to an hospital, with carcinoma of the colon, subsequently leave with any chance of surviving the disease. Some are inoperable from the outset; some die following operation; some survive the operation but harbor metastatic tumors, which cannot be eradicated. Since the inoperable cases and those having remote metastases cannot be permanently benefited, it becomes all the more important not to lose, through operative mortality, those who have a reasonable chance of cure. The results of Doctors Gibbon and Hodge's study of a representative series of cases appears to indicate that this objective will be promoted by the further development and more widespread use of aseptic anastomosis.

DR. WILLIAM B. PARSONS (New York, N. Y.): I am very glad that Doctor Gibbon has brought forward this very interesting paper and has emphasized some of the points in safe large bowel surgery.

I would like to speak for just a moment on the question of the right colon and not so much about the left colon. The niceness of the anastomosis, the niceness of the technic, and the prevention of immediate contamination is, of course, important. Unquestionably, the big danger is subsequent leakage; the main point in that is the question of decompression. Both Doctors Gibbon and MacFee spoke about the need of decompression.

At the next meeting of the American Medical Association, Doctor Leigh, of the Presbyterian Hospital, is going to report on the use of the Miller-Abbott tube. In the past two years that has been a method of real importance in reducing the operative mortality. There are several points about the employment of the tube that Dr. Leigh will emphasize in his report, one of them being that it must be introduced prior to operation, and the tube must be in the small bowel before the operation is begun. Among other points, he will report that during the past two years, at the Presbyterian Hospital in New York, with a number of men performing the surgery, the mortality without the use of the tube was 22 per cent, but with its use it was 6.7 per cent.

DR. RICHARD B. CATTELL (Boston, Mass.): This has been a very interesting discussion to me, since from our experience at the Lahey Clinic we carry out resections of the colon by means of the exteriorization principle, and since the paper of Doctors Gibbon and Hodge contrasts the two methods, it seems reasonable to present our experience in dealing with the exteriorization procedure.

Since 1929, but one case has had a primary resection, with aseptic anastomosis. The rest have all been operated upon in two stages, and 90 per cent of all resections by a modified Mikulicz plan. During this time, approximately 275 patients have had resections by employing the exteriorization procedure, with a mortality of 13 per cent. Of those followed over five years, 53.6 per cent of those resected have had no evidence of recurrence.

The slide that Dr. Gibbon showed of operability is a thing that interests us most. It was approximately 53 per cent in his group of cases. We believe that the employment of the exteriorization principle will enable us to markedly raise the operability in these

## ASEPTIC ANASTOMOSIS

cases. One will not venture to perform an intraperitoneal anastomosis with a dilated and distended bowel, because of the possibility of postoperative infection from leakage from the suture line; and it is in these cases that the exteriorization principle can be applied with reasonable safety, at least as borne out by our experience. In other words, we can offer relief to a larger number of the unfavorable cases by the utilization of this method and, furthermore, we believe it is a safe method for all resections of the colon.

DR. HARRY H. KERR (Washington, D. C.): After Doctor Cattell's talk on exteriorization, I might review some cases that were recently gathered for another presentation, where only resection was considered, with immediate mortality, without comparing the exteriorization operation, with resection.

In a study of all cases of intestinal resection performance at the Garfield Memorial Hospital in Washington, to determine the value of the aseptic technic over the open method, 107 operative records were reviewed: Sixty-eight resections had been performed by the open method and 39 by the aseptic basting-stitch technic. The list includes all resections done in that time, and of course contains many desperate cases of strangulation, intussusception, etc. Garfield is not a closed hospital and is open to all the good surgeons of the city. Therefore, the study records the work of many surgeons.

In the cases resected by the open method, there was an immediate mortality of 35 per cent. In the cases resected by the basting-stitch technic, the immediate mortality was 15 per cent.

In a review of my own private cases of intestinal resection, all done with the basting-stitch technic, I have records of 40 cases, with a hospital mortality of 12.5 per cent. That, corrected for immediate mortality by autopsy on two of the cases that died (one of uremia and another of pneumonia) would reduce the mortality to about 7 per cent. The list includes nine cases of resection for Hirschsprung's disease, with no deaths.

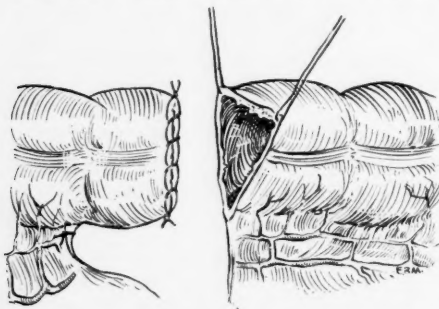
I do not think there is any question that the profession has accepted the idea that direct end-to-end anastomosis is the most physiologic and the preferred operation for resection, and I do not doubt that the Miller-Abbott tube, and possibly the sulfanilamide groups, will further reduce our mortality.

DR. WARFIELD M. FIROR (Baltimore): Rather than quote statistics, I think it may be pertinent if we ask ourselves a question: What is the cause of death in those cases in which the Mikulicz procedure is employed? It seems to be obvious that there are two main causes: First, the spread of infection when closure is attempted; and, second, the fact that the patient is hospitalized for a long period of time.

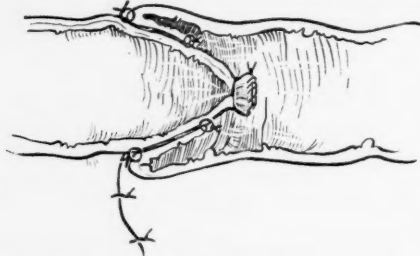
It is conceivable that the advantages of the Mikulicz procedure may be utilized and also those of an end-to-end anastomosis, if some sulfonamide compound can be found which can be used after the first stage of the Mikulicz procedure. We have had six cases in which sulfanilylguanidine has been so employed; and in every instance with an intact mucuous membrane following the removal of the growth, the bacterial count has fallen to an insignificant number. We have felt justified, therefore, in performing an end-to-end anastomosis and replacing the intestine in the peritoneal cavity, thereby shortening the period that is required for closing the bowel in the ordinary Mikulicz operation.

DR. LEO ELOESSER (San Francisco): There is a difference between carcinomata of the lower bowel, with obstructive symptoms and those without. It may be best to treat carcinomata with obstruction by resection and exteriorization of the afferent loop, and those without obstruction by resection and immediate anastomosis. An invagination operation, which is a compromise between Kerr's aseptic anastomosis and an open operation, is simple and satisfactory both for immediate anastomosis and closure of a colostomy. Resection is performed aseptically, between clamps. The upper segment is closed by a fine catgut suture, its mesentery is freed for about one inch or one inch and one-quarter back from the site of resection, the triangle formed by the two leaves of the mesentery and the bowel wall is closed by a fine catgut suture. The closed upper segment is then invaginated into the lower segment and the two are united by one or two layers of sutures through their serous and muscular coats. The upper segment thus hangs into the lower one like a cervix into the vaginal vault. Recently, I have closed the upper segment by a fine catgut suture that approximated the two opposing mucous coats instead

of putting in a basting-stitch approximating the serosa. This mucous stitch holds for a few days only; the basting-stitch through the serous coat has kept the bowel closed so long that I often feared it never would open. Although the lower segment is opened momentarily while the upper one is invaginated into it, contamination is minimal, for the upper segment is kept aseptically sealed throughout.



(a) Afferent limb closed, ready for invagination.



(b) Cross-section of completed anastomosis.

the collected series here, of 246 cases, gave approximately the same mortality with the aseptic method. Thus the exteriorization method in expert hands certainly does give an adequately low mortality.

DR. JOHN H. GIBBON, JR. (Philadelphia, closing): In regard to a point which was raised by Doctors Firor and Cattell, we have the conviction that it is a mistake to perform any operative procedure upon the tumor in the case of obstruction. We think that the ideal preliminary procedure in obstruction of the left colon is a transverse colostomy or cecostomy. In lesions in the right colon, a preliminary decompression is rarely necessary. If a decompression is done and the bowel cleaned, all cases, then, are readily susceptible to primary anastomosis. In our series we found that when exteriorization was done in the face of obstruction there was often a great deal of trouble.

I was interested to see that Doctor Cattell's mortality at the Lahey Clinic was 13 per cent with the exteriorization method, and



## CHRONIC ULCERATIVE COLITIS\*

A SUMMARY OF EVIDENCE IMPLICATING *BACTERIUM NECROPHORUM*  
AS AN ETIOLOGIC AGENT

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IT IS THE PURPOSE of the present communication to present a summary of a study on the problem of chronic ulcerative colitis carried on as a joint enterprise in the Departments of Surgery, Bacteriology, and Medicine of the University of Chicago during the past eight years. Most of the data presented in previous reports<sup>3</sup> has been confirmed in our further experience and considerably amplified. As a result of this work we are persuaded that *Bacterium necrophorum*, together with factors, some of which are at present unknown, plays an etiologic rôle in the disease.

It has long been recognized that the part played by bacterial infection in chronic ulcerative colitis, as in other enteric infections, has been difficult of solution to a large extent because of the extraordinary variety and abundance of the normal intestinal flora. The nature of the bacterial species in the various levels of the normal gastro-intestinal tract and their relative abundance has been found to depend among other things on the type of organisms ingested with the food, the presence of foci of infection in the nose and mouth, the acidity of the gastric secretion, the rate of passage of the fecal current, and perhaps of greatest importance on the character of the diet. It is small wonder, then, that cultures taken from the colon discharges or from lesions, seen with the proctoscope, in patients with chronic ulcerative colitis have yielded a wide variety of organisms and little agreement among investigators.

A number of years ago, in a study of the problem of acute intestinal obstruction, one of us together with Moorhead and Burcky<sup>1</sup> made the observation that segments of the intestine isolated from continuity with the alimentary tract but retaining their normal blood supply become sterile after the passage of time. Thus, a segment of jejunum or ileum, isolated as in Figure 1, and washed with sterile water to remove solid material, becomes sterile in a few weeks if dropped back into the peritoneal cavity. Dack<sup>2</sup> has similarly observed that such segments drained to the outside as in the Thiry-Villa fistula also become sterile if undisturbed by the trauma of irrigation or injection. The factors involved in this self-sterilization seem to be

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chiefly mechanical and consist in the protective action of the intestinal mucus, which entangles the organisms, and peristalsis which steadily propels them along the tube. It occurred to us then that a study of the bacteria in the colon of patients with chronic ulcerative colitis ought to be more significant when the diseased colon is isolated from the fecal stream and the processes of self-sterilization are operative, in which case the organisms that might be found to persist ought to be of greater significance than the birds of passage.

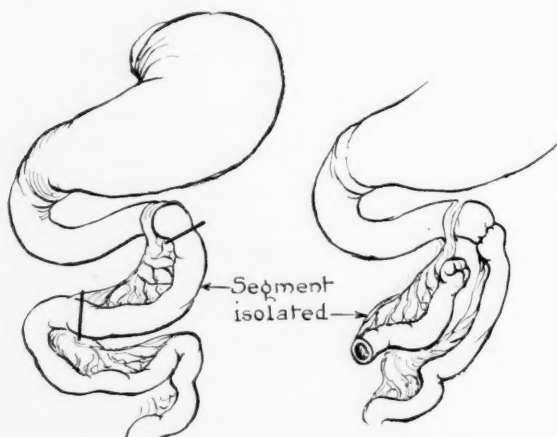


FIG. 1.—Diagram illustrating an isolated segment of jejunum sterilized by prolonged drainage into the peritoneal cavity.

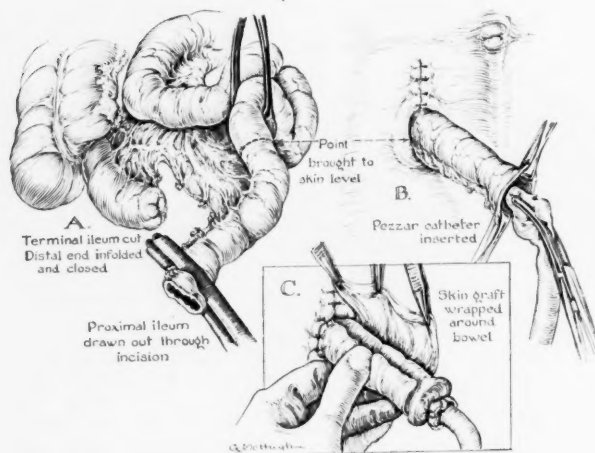


FIG. 2.—Diagram illustrating a method for end-ileostomy.

It is not our purpose to discuss the merits of ileostomy in the treatment of chronic ulcerative colitis. It is our conviction that the procedure is definitely beneficial when so performed that irritation and digestion of the abdominal wall does not occur. The method that we have employed will be presented in detail elsewhere and a short description will suffice here (Fig. 2). The abdomen is opened through a short, low right rectus incision. The ileum

is transected about four inches from the cecum and the distal end closed. The mesenteric vessels supplying the lower six inches of the proximal end of ileum are divided about an inch from the point where they enter the intestinal wall, in order to preserve the distal arcade and thus prevent necrosis of the portion of ileum that is to be exteriorized. The ileum is then brought out six inches beyond the skin surface and the wound closed loosely, with the mesenteric

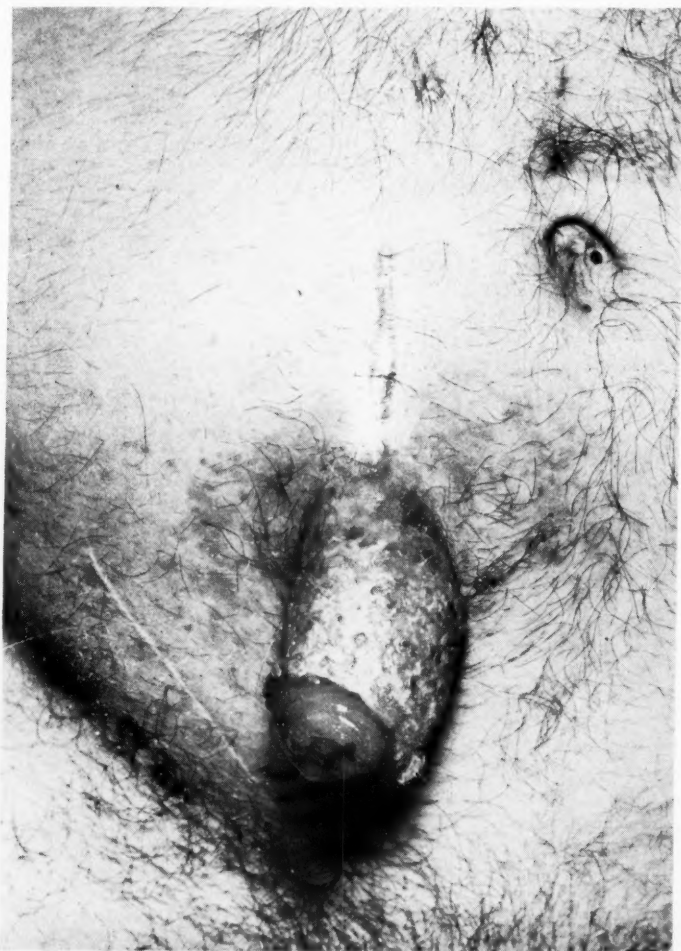


FIG. 3.—Photograph showing appearance of the skin-covered ileostomy three months after the operation. Note the absence of excoriation of the surrounding skin.

border sutured at the lower end of the incision so that the exteriorized ileum will arch downward. A small Pezzar catheter is then tied into the lumen of the bowel to drain off the intestinal content. A rectangular segment of skin, four by eight inches in size and six one-thousandths of an inch thick is then cut from the neighboring abdominal wall with a Padgett dermatome and wrapped carefully around the exteriorized portion of ileum suturing it only

to the skin of the abdominal wall which surrounds the fistula. A gauze pressure-dressing completes the operation. The Pezzar catheter usually remains intact for six days when the dressing may be removed. A complete take of the graft has occurred in the four cases where we have employed this

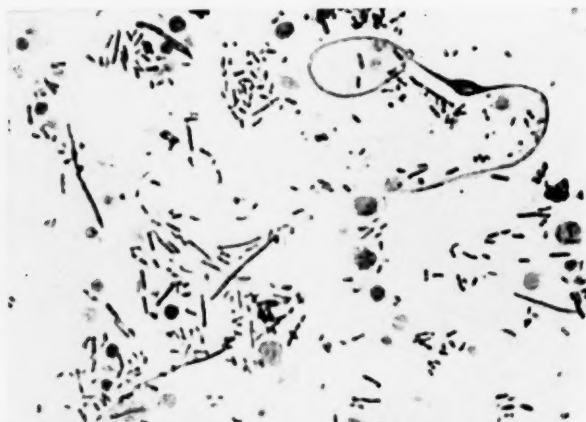


FIG. 4.—Photomicrograph showing a pure culture of *Bacterium necrophorum* from an anaerobic blood agar plate. ( $\times 2,700$ )

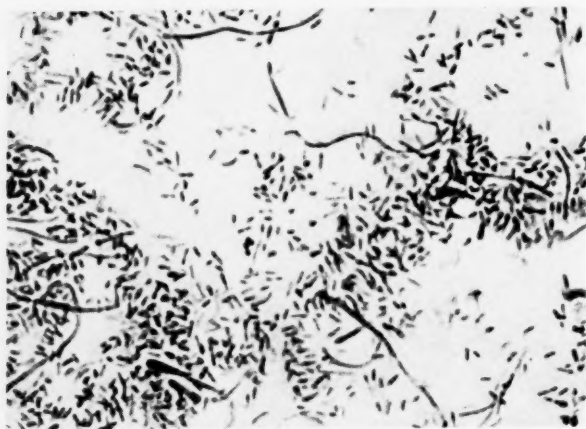


FIG. 5.—Photomicrograph showing the characteristic morphology of *Bacterium necrophorum*, pleomorphism and filamentous forms. ( $\times 2,700$ )

procedure. The resulting ileostomy looks somewhat like a penis and may be easily fitted with an ileostomy bag. The absence of excoriation of the skin is illustrated in the photograph in Figure 3.

At the present time, we have data on the bacteriology of the colon in 12 patients with chronic ulcerative colitis in whom the fecal current has been diverted by end-ileostomy. The symptomatology, roentgenographic and proctoscopic observations were in each case characteristic of the severe form of the disease. All had been treated in the Medical Service for varying periods of time, and were finally referred for surgical treatment because of

progressive cachexia, anemia, and persistence of local symptoms. Cultures from saline washings of the colon were secured before operation, at weekly intervals for the first two or three months afterward, and at irregular intervals during the following years. A strikingly similar result was observed in all. With the diversion of the fecal current, aerobic organisms began to diminish

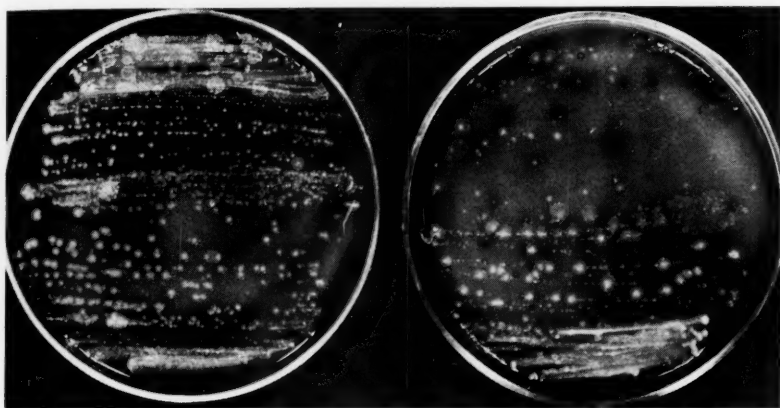


FIG. 6.—Anaerobic blood agar plate from a swab culture secured at proctoscopic examination from an area of colon acutely ulcerated in a patient with chronic ulcerative colitis. The colonies with dark rings about them are *Bacterium necrophorum*.

FIG. 7.—Anaerobic plate showing a culture from the same patient as in Figure 6, but taken from an area of mucosa not actively involved. No colonies of *Bacterium necrophorum* are present.

steadily in number and after five to six weeks the flora became almost entirely composed of nonsporulating anaerobes.<sup>3</sup> Careful examination of the anaerobic plates revealed a progressive predominance of one organism producing grayish raised colonies from 0.5 to 1 Mm. in diameter. The blood agar surrounding the colonies was unchanged in the anaerobic state but took on a green color when exposed to air. A foul odor was produced. Stained preparations show this organism to be a gram-negative pleomorphic rod, with occasional filamentous forms and irregular staining, but with no true branching and no spores (Figs. 4 and 5). It grows only in a strictly anaerobic environment and is easily killed by exposure to oxygen. In one patient with chronic ulcerative colitis several enlarged lymph nodes in the mesentery of ascending colon were removed at the time of the ileostomy, and from these the organism was secured in pure culture. It was isolated from the colon of a young girl who died of ulcerative colitis and also from a thrombus in the portal vein at the hilum of the liver. In the patients with ileostomies the organism was, as a rule, easily recovered during periods of acute exacerbation, when blood and pus were present in the colon discharge, but was not found, or only with difficulty, during periods of quiescence. In one of these patients, the colon was resected three years after the ileostomy was produced, and at this time the organism was still predominant in the diseased colon. It was also isolated together with an anaerobic streptococcus from a mesenteric lymph node in this resected specimen.



We have called the organism *Bacterium necrophorum* because it seems to be identical with the *Bacillus necrophorus* isolated by Bang, in 1890, from cases of calf diphtheria. Bang's organism is well known among veterinarians as the cause of necrotizing lesions in nearly all domestic and in some wild animals, *i.e.*, calf diphtheria, necrotic ulcers of the colon in hog cholera, metastatic necrosis of the liver and lungs of cattle and swine, necrotic stomatitis of calves, lambs, and pigs, and necrotic lesions in the skin of sheep. It is also probably identical with the *Bacillus funduliformis* described by Hallé,<sup>4</sup> Lemierre,<sup>5</sup> and other French workers, and found to be the cause of ulcerative lesions about the mouth and subsequent often fatal septicemias. Henthorne, Thompson, and Beaver,<sup>6</sup> of the Mayo Clinic, have isolated *Bacteroides funduliformis* in pure culture from four cases of hepatic abscess secondary to carcinoma of the rectum. Their organism seems to be identical with our *Bacterium necrophorum*. Similar organisms have been recovered before from liver abscesses, notably by Harris,<sup>7</sup> Cunningham,<sup>8</sup> and Norris.<sup>9</sup>

During the past eight years, *Bacterium necrophorum* has been obtained from about 70 per cent of the patients with chronic ulcerative colitis in our clinic. Two hundred and ninety-eight patients with all stages of the disease have been examined during this period. The organism is difficult to cultivate and a routine technic is not apt to be successful. This is due to the extreme sensitivity of the organisms to oxygen and to the tendency of the fecal bacteria to overgrow the plates. Swabs taken from ulcerated areas by means of the proctoscope and immediately streaked on the surface of 10 per cent sheep blood-veal infusion agar plates, which are then incubated under strict anaerobic conditions, have usually been successful. Our failures to demonstrate *Bacterium necrophorum* in patients with chronic ulcerative colitis have occurred, as a rule, during periods of temporary recovery or quiescence or when it was not possible to make repeated cultures (Figs. 6 and 7). Ninety-nine normal individuals were examined with a similar technic but in none of these was *Bacterium necrophorum* found. It was, however, recovered from two patients with carcinoma of the rectum, from one case of lymphogranuloma inguinale, and from one patient with an inflammatory stricture in the sigmoid.

The various strains of *Bacterium necrophorum* isolated from different cases of ulcerative colitis have displayed a similar bizarre morphology and cultural characteristics, but some differences in antigenic properties. Thus, rabbits injected with one strain develop agglutinins to the specific organism injected in much higher concentration than to strains from other sources. Perhaps, the best evidence implicating *Bacterium necrophorum* as an etiologic agent in ulcerative colitis has been the discovery of specific antibodies to this organism in the blood of patients with the disease but not in normal individuals. Both complement-fixing antibodies and agglutinins have been demonstrated. Specific agglutinins for *Bacterium necrophorum* have been found regularly in the blood of ulcerative colitis patients and usually in higher concentration during the active stages of the disease (Table I). In each case, also, a higher concentration of agglutinins for the patient's own strain of

# ULCERATIVE COLITIS

*Bacterium necrophorum* has been found than for strains from other individuals. This is well illustrated in Table II, where the serum of patient No. 159, in dilutions as high as one in 640, agglutinated strains of *Bacterium necrophorum* obtained from her own colon but had no effect on strains of the same organism from other patients. The presence of these specific antibodies strongly suggests that the organism is actively implicated in the disease process since agglutinins were not found for various strains of *B. coli*, also isolated from the contents of the diseased colon.

TABLE I

PATIENTS\* WITH CHRONIC ULCERATIVE COLITIS. CORRELATION OF SEVERITY OF DISEASE AS DETERMINED BY PROCTOSCOPIC APPEARANCE WITH PRESENCE OF BACTERIUM NECROPHORUM AND WITH AGGLUTININS FOR BACTERIUM NECROPHORUM

Proctoscopic Appearance	Number of Patients	Number from which <i>Bacterium necrophorum</i> Cultured	Number Patients with Agglutinin Titer of 1-40, or Higher, for One or More Antigens
0	5	1	1
1	11	2	4
2	18	7	8
3	18	9	13 (one not tested)
4	13	11	9 (two not tested)

Proctoscopic key:

0 = healed or normal mucosa.

1 = finely granular mucosa—slight contact bleeding in one or several areas.

2 = granular mucosa; contact bleeding—areas with no inflammation.

3 = bleeding granular mucosa. Little exudate, areas with less marked involvement.

4 = markedly inflamed; bleeding friable mucosa; purulent exudate.

\* Thirty-six patients were tested, several of them repeatedly, over a period of months during different stages of disease.

TABLE II

AGGLUTININS IN SERUM OF THREE PATIENTS TO HOMOLOGOUS AND HETEROLOGOUS STRAINS OF BACTERIUM NECROPHORUM

Patient (Strain)	Date	Proctoscopic Appearance	Agglutinin Titer of Serum for Strains of <i>Bacterium necrophorum</i>					
			103	146	152	159	161	164
H. A. (164)	1/6 /39	1		0		0	0	0
	2/10/39	3		0		40	0	0
	2/24/39	4		0		0	80	80
	6/2 /39	2	0	40	80	0	160	80
L. D. (161)	12/10/38	4				0	80	0
	1/17/39	4				0	80	40
	5/2 /39	4	0	80	160	0	160	40
I. K. (159)	12/20/38	4				640	0	0
	2/14/39	4				160	0	0
	4/4 /39	3	0	0	0	320*	0	0

\* Serum not tested above this dilution.

The available data indicate that *Bacterium necrophorum* is pathogenic for both man and the lower animals. Under the names *Bacillus* or *Bacteroides funduliformis* it has been implicated as the causative organism in ulcerated lesions in the throat and metastatic abscesses in distant organs.<sup>5</sup> We recovered it in pure culture from a chronic breast abscess, and have received cultures of the organism, isolated by others, from a case of osteomyelitis of the femur secondary to middle ear infection, two cases of pleural empyema, and from the blood stream of a patient with lung abscess. We have also

repeatedly isolated it in pure culture from liver abscesses in cattle. The strains of *Bacterium necrophorum* that we have recovered from cases of ulcerative colitis are pathogenic for rabbits, producing in them chronic abscesses on subcutaneous injection. Strains secured from liver abscesses in cattle are more virulent for rabbits than those of human origin and a fatal spreading cellulitis is easily produced. We have, however, been unsuccessful, to date, in reproducing chronic ulcerative colitis in any of the lower animals. Pure cultures of *Bacterium necrophorum* have been given by mouth or by rectal injection, and have been introduced into isolated segments of the colon and lower intestine in dogs, monkeys, and baboons, without the development of any lesions. However, the instillation of a large amount of the bloody purulent discharge from the colon of a seriously ill patient into the same animals was also without effect.

This inability of *Bacterium necrophorum* to set up a colitis under the conditions of our experiments is not surprising in view of some aspects of the epidemiology of the disease. It does not occur in epidemics and is not transmitted even by closest contact. One of our patients, a young woman in whom an ileostomy was performed subsequently gave birth to a healthy baby, and neither husband nor child developed the disease, although the isolated colon of the mother continued to harbor *Bacterium necrophorum* and continued to discharge blood and pus. These observations suggest that the causative agent is not markedly invasive or that some special susceptibility of the host is essential. The excessive chronicity of the disease and its refusal to heal completely even during periods of comparative good health are likewise factors to be considered. Here, too, certain of the properties of *Bacterium necrophorum* appear significant. Beveridge<sup>10</sup> was unable to demonstrate the development of immunity to this organism in rabbits and we have confirmed this observation in a more extensive study.<sup>3</sup> Rabbits immunized by repeated injection of *Bacterium necrophorum* developed chronic subcutaneous abscesses as readily and as extensively as the controls. The local necrotizing action of this organism and its failure to incite an increased resistance in the host correspond with the pathology in the colon and the long clinical course of the disease.

#### SUMMARY

(1) When the seriously diseased colon in patients with chronic ulcerative colitis is isolated from the fecal stream, as by end-ileostomy, aerobic organisms disappear and anaerobic organisms persist in large numbers in cultures secured by swabs or saline washings of the lower sigmoid. Since the isolated colon remains diseased for years, it seems probable that the responsible organism or organisms are anaerobic in nature.

(2) The following evidence indicates that *Bacterium necrophorum* plays an etiologic rôle in the disease:

(a) It is the predominant organism in the isolated colon in ulcerative

colitis during periods of exacerbation and tends to disappear during periods of spontaneous quiescence.

(b) It has been found in the great majority of cases of typical ulcerative colitis when appropriate methods for its detection have been used.

(c) Specific antibodies for this organism have been found in the blood in cases of chronic ulcerative colitis and not in the blood of normal individuals.

(d) The organism is pathogenic for rabbits, producing in them local abscesses and for man as indicated by its isolation in pure culture in a wide variety of pathologic processes.

(e) Examination of the literature indicates that it is very similar if not identical with *Bacillus* or *Bacteroides funduliformis* which has been repeatedly found associated with necrotic lesions of the mucous membranes in man and with *Bacillus necrophorus* which is thought to cause various necrotic lesions in domestic animals.

(3) *Bacterium necrophorum* is probably present in the normal alimentary tract of man and monkeys and requires some additional factors producing necrosis of the mucosa to furnish conditions suitable for its growth. Once this occurs, the organism seems capable of continuing and extending the process.

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DISCUSSION.—DR. FRANK L. MELENEY (New York, N. Y.): We have been very much interested in the work of Doctors Dragstedt and Dack in this field, and we believe that they have demonstrated the importance of *Bacterium necrophorum* in certain cases of ulcerative colitis. They do not claim that it is the etiologic agent, and I believe that we still have to reserve judgment on that point. I think the fact that they have demonstrated that it persists in the isolated colon after practically all of the other organisms have disappeared is significant. I also believe that the presence in the patients' serum of agglutinins against their own organism, of a higher titre than against other strains of the same species, likewise indicates that at least some of the antigenic properties of the organism have been absorbed from the colon.

Of course, in a field which is normally so completely contaminated by many strains of bacteria, as the intestine is, it is very difficult to prove which one, if any, is the significant organism as a causative agent with respect to ulceration of the bowel.

Since Doctors Dack and Dragstedt first published their work we, in our laboratory, have been searching for these organisms in cases of chronic ulcerative colitis. Our habitual search for anaerobes in all specimens that come to the laboratory has also given us the opportunity to find *Bacterium necrophorum* in our cultures from other lesions. Although we have tried very hard to find them in our cases of ulcerative colitis, carefully searching for them in 40 cases which we have examined, we have found them in only three. On the other hand, we have found them in nine other lesions which I would like to enumerate:

(1) In a chronic ulcer of the vagina in a little girl, associated with an anaerobic streptococcus. (2) In a deep pelvic abscess, associated with an anaerobic streptococcus and a *Staphylococcus albus*. (3) In a carbuncle, associated with *Staphylococcus aureus*. (4) In an appendiceal abscess, associated with a colon bacillus, and an anaerobic streptococcus. (5) In a sacrococcygeal cyst, associated with an anaerobic streptococcus. (6) In a thyroglossal cyst abscess, in pure culture, without extensive necrosis of tissue. (7) In a face infection following a dental abscess. (8) In a liver abscess. (9) In a postgastrectomy wound infection.

Doctor Dragstedt has stated that the organism is very susceptible to oxygen; we have confirmed that finding. On account of the probability that anaerobic organisms play a rôle in ulcerative colitis, we have advocated local treatment with zinc peroxide. In the three cases of ulcerative colitis in which we found the *Bacterium necrophorum*, we have had a favorable response to treatment with zinc peroxide. In one of these cases we have been able to keep the disease in a quiescent phase. The patient feels entirely normal with the nightly use of zinc peroxide as a retention enema. In another desperately sick case, rectal administration was not enough. We performed a cecostomy, and delivered the zinc peroxide through the cecum. The disease in the upper large bowel was completely controlled as revealed by a subsidence of symptoms and the restoration of normal contours, as shown by barium enema, but disease persisted in the rectum. A temporary left lower quadrant colostomy was then performed; the fecal stream cut off from the rectum; and this was treated with zinc peroxide, with complete subsidence of the inflammation and healing of the ulcerations. The continuity of the intestine will be restored if the lower segment remains normal for a year.

In the third case, zinc peroxide was delivered through a cecostomy and the upper large bowel was restored to normal. An abdominoperineal operation was performed for persistent rectal involvement and anal fistulae. That patient has remained perfectly well for over three years, with apparent restoration of normal bowel above the level of the colostomy.

I believe zinc peroxide should be considered in treating cases of ulcerative colitis, conservatively at first from below, as a retention enema. If the case does not respond to that, there should be either a cecostomy or in very bad cases, an ileostomy is performed to cut off the fecal stream. If it is delivered from above, serious cases may be restored to normal.

There seems to be a real chance to restore the bowel and avoid an extensive resection. In some cases it may still be necessary to remove the rectum if its mucous membrane has been completely destroyed.

DR. LESTER R. DRAGSTEDT (Chicago, closing): I should like to emphasize that *Bacterium necrophorum* is probably identical with *Bacillus funduliformis* isolated by Lemierre and Hallé from ulcerative lesions in the nose and throat, with secondary septicemia and metastatic abscesses in distant organs. It is likely that the organism is a normal inhabitant in the alimentary tract. We have, however, so far been unable to isolate it from the colon of normal individuals. This may be because it is so difficult to isolate and cultivate on the ordinary media. In view of the relatively slight invasive properties of *Bacterium necrophorum*, it seems probable that some other agent may first induce acute ulceration in the colon which is then extended and maintained by the necrotizing properties of *Bacterium necrophorum*. This name seems preferable to *Bacillus funduliformis* because of priority, having been first suggested by Bang, in 1890.



## INTESTINAL ANTISEPSIS, WITH SPECIAL REFERENCE TO SULFANILYLGUANIDINE\*

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BALTIMORE, MD.

IN APRIL, 1940, Roblin and his associates<sup>1</sup> described the synthesis and physical properties of sulfanilylguanidine before the Division of Medicinal Chemistry at the meeting of the American Chemical Society. These investigators gave the solubility of the compound in water as 190 mg. per 100 cc. at 37° C. Despite this relatively high solubility, they found that the chemotherapeutic activity, as tested in mice, to be considerably less than that of the active sulfonamides. In September, 1940, E. K. Marshall, Jr., *et al.*,<sup>2</sup> published a report of their experiments with sulfanilylguanidine. They had studied its antibacterial properties and its absorbability when given orally and intraperitoneally. They also described their observations on the toxicity of this compound in laboratory animals. These studies led them to conclude:

- (1) "Although fairly soluble in water, sulfanilylguanidine is poorly absorbed from the intestinal tract.
- (2) "The concentration of coliform bacteria in the feces of mice can be reduced by its administration.
- (3) "The toxicity of this drug has been investigated in mice, rabbits and dogs. On the basis of all experiments, it would appear, when given by mouth, to be no more, and probably less, toxic than sulfapyridine and sulfathiazole."

Believing that an antibacterial compound, which is fairly water soluble but only slightly absorbed from the intestine, would be of great value in surgery, we gave sulfanilylguanidine to 12 patients who required operations upon the colon. The results of this initial study were presented<sup>3</sup> at the meeting of the Southern Surgical Association in December, 1940. None of the patients showed detectable evidences of toxicity. In some cases, the fall in the concentration of coliform organisms in the stool was surprisingly great and, although no conclusions were drawn from such a limited experience, the impression was gained that this drug is an adjuvant in colonic surgery. Further clinical experience with the use of this sulfonamide, modified the initial impression and made experimental work necessary in order to ascertain the value of this drug in surgery. The results of our studies with sulfanilylguanidine can be most conveniently presented under the appropriate headings: (1) Reduction of coliform bacteria in the stool; (2) absorption and excretion of the drug; and (3) toxicity.

(1) *Reduction in the Coliform Bacteria in the Stool.*—Our observations upon patients had not progressed very far before it became clear that in some

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

persons the number of coliform organisms in the stool was unaltered despite the oral administration of sulfanilylguanidine for ten days. The regular dose was 50 mg. per kilo of body weight, every eight hours. On the other hand, there were patients in whom the drug produced an impressive reduction in the number of these bacteria in the stool. Similar variations in the response to this drug were observed in dogs; in fact, with twice the dose, *i.e.*, 50 mg. per kilo, every four hours, it was the exceptional animal that had even a moderate lowering in the concentration of the coliform bacteria. When dogs were kept on a low residue diet and given 1 Gm. of the drug per kilo per day, in six equal doses by gavage, a marked reduction in the bacterial count usually occurred in

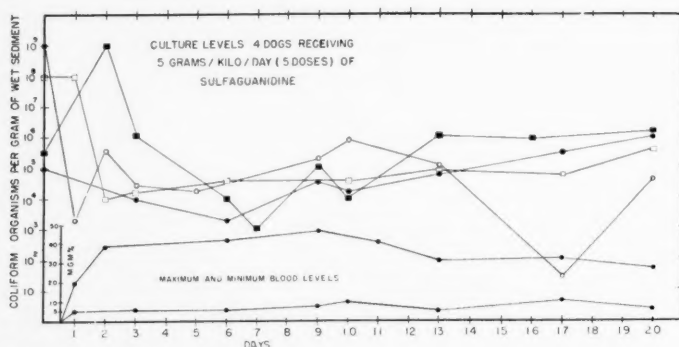


CHART 1.—The effect of large doses of sulfanilylguanidine on the number of coliform organisms in the stool of dogs. The maximum and minimum concentrations of the drug in the blood are shown.

from five to eight days. There were some dogs, however, under this regimen that failed to show a definite reduction, and a further increase in the dose would sometimes, but not always, cause a significant lowering in the number of bacteria in the feces. There were many animals that survived the incredibly large dose of 5 Gm. per kilo per day for more than a month. Chart 1 illustrates the course of four such dogs. It is seen that the concentration of coliform organisms is gradually reduced to a level varying from 10,000 to 100,000 organisms per cc. of wet sediment of stool, and that further reduction is not attained by continued administration of the drug.

On theoretical grounds, if the bacteriostatic effects of sulfanilylguanidine are due entirely to the action of the drug on the contents of the bowel, then it follows that the maximum effect should be expected when saturation of the intestinal contents is reached. In an effort to throw light on this point, the concentration of sulfanilylguanidine in the stool was determined and correlated with the bacterial count. No relationship could be established because the stool always contained solid drug if more than 0.5 Gm. per kilo per day was given by mouth, and it was found that this was the minimum amount required to lower the bacterial count. In dogs which received enormous amounts of the drug by mouth, the feces would be almost solid with sulfanilylguanidine; yet, 1 cc. of the wet sediment of such a stool frequently contained over 100,000 coliform organisms.

# SULFANILYLGUANIDINE

The bacterial count in the stool may not represent an accurate indication of the action of sulfanilylguanidine within the colon. It seems that the repeated analysis of the contents of isolated segments of colon that contained the drug

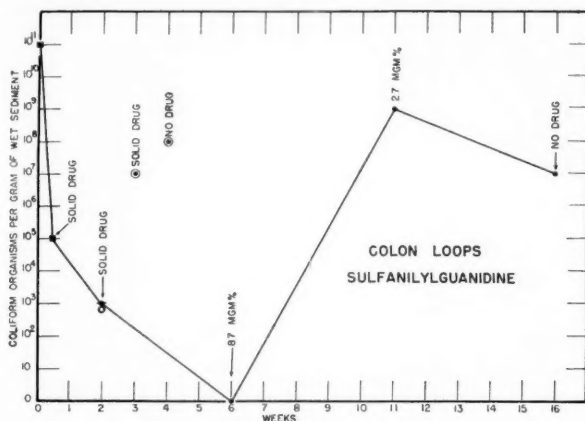


CHART 2A.—The rate of absorption and the bacteriostatic effect of sulfanilylguanidine when placed in isolated colonic loops.

might give more reliable data. Our next experiment was planned to do this and also to compare the antibacterial effect of sulfanilylguanidine and sulfanilamide under standard conditions.

For this purpose, identical segments of the colon of dogs were isolated and the continuity of the bowel was restored by anastomosis. From each isolated segment the gross fecal matter was washed away, specimens for bacteriologic study were taken, and 5 Gm. of either sulfanilamide or sulfanilylguanidine were placed in the lumen of a loop before closure was completed. Subsequently, the peritoneal cavity was opened and the contents of the loop were aspirated under aseptic precautions. The samples thus obtained were studied to determine (1) the concentration of the drug remaining in the loop; and (2) the effect of each compound on the bacteria within the loop.

The values found in these determinations are given in Chart 2 A and B. Under the conditions of this experiment it is evident that each compound caused a pronounced decrease in the number of coliform bacteria within the lumen of the isolated segments of colon. The fall in the number of bacteria extended from over a billion organisms per cc. to less than ten. In every instance, the bacteriostatic effects disappeared when all the drug had

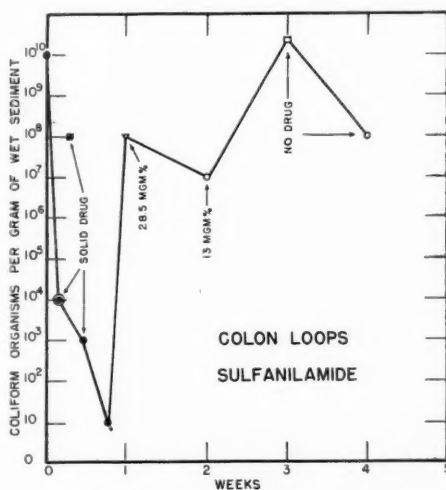


CHART 2B.—The rate of absorption and the bacteriostatic effect of sulfanilamide when placed in isolated colonic loops.

been absorbed from the loop. From the charts, it is clear that the rate of absorption of sulfanilamide from the isolated colonic loop is very much faster than that of sulfanilylguanidine. Histologic examination of the isolated segments of the colon did not show any alteration because of their prolonged contact with these drugs.

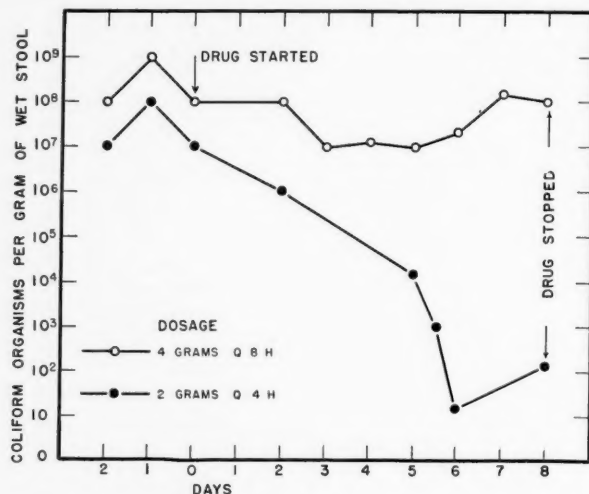


CHART 3.—The action of sulfanilylguanidine on the bacterial flora of the normal gastro-intestinal tract of man when given at four- and eight-hour intervals.

The frequent failure of sulfanilylguanidine to reduce the number of coliform bacteria in the stool might be explained on the spacing of the doses. To investigate this possibility, we gave a group of normal adult men 4 Gm. of the drug by mouth every eight hours, and a second similar group 2 Gm. of the drug by mouth every four hours. Chart 3 illustrates the differences resulting when the more frequent doses were given. It will be noticed that after eight days of treatment with an eight-hour interval, the bacterial count was scarcely altered, whereas within six days with an interval of four hours between the doses, the count fell from 10,000,000 to less than 100 organisms per cc. of stool. The greater effectiveness of frequent doses was also shown in dogs. A typical illustration is given in Chart 4, wherein the maximum effect of sulfanilylguanidine was obtained in four days when the drug was given at four-hour intervals. In contrast to this, the fall in the number of bacteria was slower and less marked when the doses were spaced at 12-hour intervals. The explanation which is offered for the greater effectiveness of the drug when administered frequently is that by shortening the interval between doses, more constant contact is maintained between the drug and the mucous membrane harboring the bacteria.

In an effort to determine why some patients showed a reduction in the bacterial count, whereas others on the same dietary regimen and dosage of sulfanilylguanidine showed no reduction, we studied the records of 48 patients

# SULFANILYLGUANIDINE

treated with the drug. From this study, it was evident that the patients with an ulcerative carcinoma in the colon showed little or no fall in the number of bacteria in the stool (Chart 5). This was consistently true and, although the number of patients with ulcerative lesions is less than 20, it is important to learn whether this observation is confirmed. If it is true that an ulcerative lesion in the bowel neutralizes the bacteriostatic activity of sulfanilylguanidine,

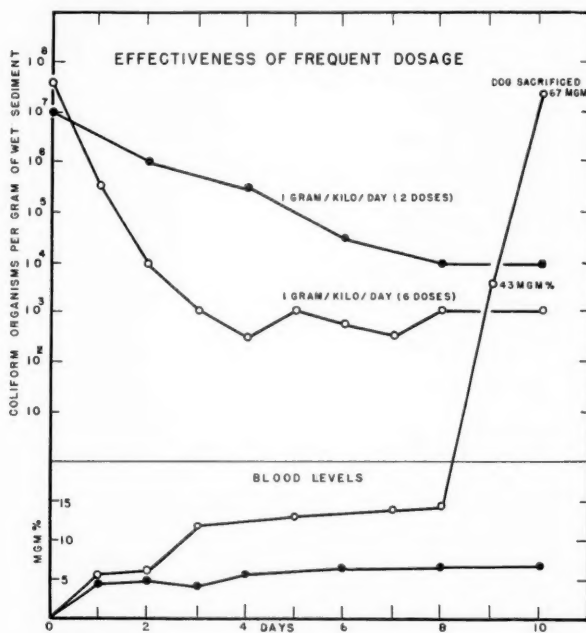


CHART 4.—The action of sulfanilylguanidine on the coliform bacteria in the gastro-intestinal tract of dogs given at four- and 12-hour intervals. The corresponding concentrations of the drug in the blood are given.

this fact will constitute a real limitation to the use of the drug in surgery. It is well known that purulent exudates contain an antisulfonamide factor which renders this compound ineffective. The suggestion is made that infected carcinomata in the bowel may produce a similar antisulfonamide factor. In our group of patients, extensive reduction in the number of coliform organisms was obtained only in those whose intestinal mucosa was intact. It was in these patients that the bacterial counts fell from over 10,000,000 to less than 1,000. If, when resecting the colon, enormous reductions are dependent upon an intact mucous membrane, surgeons may prefer a two-stage operation, in which the ulcerative lesion is removed by the Mikulicz procedure, and sulfanilylguanidine given to reduce the bacterial flora before the continuity of the bowel is restored. If sulfanilylguanidine, or a similar sulfonamide compound, can be relied upon to render the colon relatively free of pathogenic bacteria, the bowel can then be anastomosed and returned to the peritoneal cavity.



(2) *Absorption and Excretion of the Drug.*—Our experiments indicate that sulfanilylguanidine is more slowly and less completely absorbed from the intestinal tract than many other compounds of the sulfonamide series, but it has become clear that the low concentration of the drug in the blood is not due primarily to poor absorbability but rather to its prompt elimination by the kidneys. This fact is supported by the observations of Marshall and his associates,<sup>4</sup> who found that a dog receiving 0.02 Gm. per kilo of the drug by mouth had excreted 37.7 per cent after four hours, and 52.2 per cent after six hours. In a patient who received 2 Gm. of sulfanilylguanidine every four hours, the

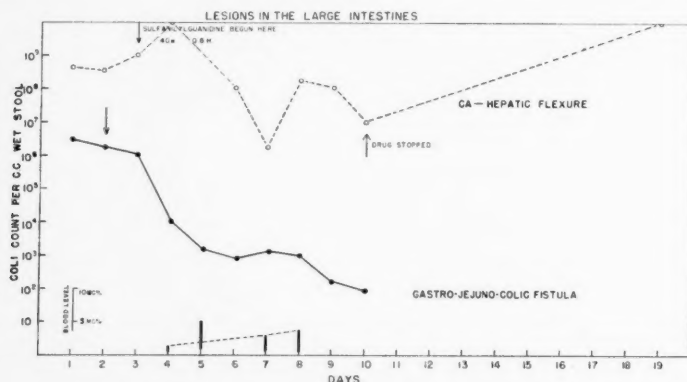


CHART 5.—The effect of sulfanilylguanidine on coliform organisms in the presence of ulcerating lesions (carcinoma of the hepatic flexure) as compared to the effect when the mucosa is intact (gastrojejuno-colic fistula).

blood level varied from 2 to 6.9 mg. per cent. On the fourth day, the total urinary output was 4.4 Gm., and during the following 24 hours more than 50 per cent of the ingested drug was excreted by the kidneys (Chart 6). Within one day after withdrawal of the drug, the renal output of sulfanilylguanidine fell to 0.05 Gm., although a considerable quantity of the drug was still in the lower colon. This bears out Marshall's<sup>4</sup> experiments, which showed that sulfanilylguanidine is absorbed from the small intestine more rapidly than from the large, and that it is promptly excreted in the urine. In this communication, dealing with the use of the drug in bacillary dysentery, it is pointed out that in one patient who received 0.05 Gm. per kilo every four hours, the average urinary excretion of the drug was 13 per cent of the amount ingested. In a second patient, on the same dosage, the average excretion was 25 per cent. It is noteworthy that these patients (Cases 5 and 7), were having diarrhea, and that the patient with the 25 per cent urinary excretion was having from seven to ten stools a day.

It must be emphatically stated that absorption from a diseased intestine, or in the presence of intestinal obstruction, is unpredictable. To demonstrate this, the following experiment was performed: The terminal ileum of dogs was divided and occluded. One gram of sulfanilylguanidine per kilo was introduced into the intestine above the obstruction. The results in the blood levels varied from 3 to 350 mg. per cent. The animal which showed the latter figure

died within four hours. In patients with actual or impending intestinal obstruction, the use of sulfanilylguanidine is contraindicated, for not only is the absorbing function of the intestine greatly altered but the occurrence of reversed peristalsis tends to retain the drug in the small intestine, where it is readily absorbed.

In several of the animal experiments, in which from 1 to 5 Gm. of sulfanilylguanidine per kilo were administered each day over a period of weeks, a sudden increase in the concentration of the drug in the blood occurred. An illustration of this complication is shown in Chart 4. Whether this is due to an alteration in the rate of absorption or excretion of the drug is not clear, but the latter seems more probable. Similar observations have

not been made in patients, but, on the other hand, the drug was always withdrawn on the first evidence of toxicity. It seems likely that, with the customary therapeutic dose of sulfanilylguanidine, patients with severe renal disease or those having anuria following anesthesia, might develop excessively high blood levels. It is imperative, therefore, that the renal function of a patient be fairly normal before he receives this drug.

(3) *Toxicity.*—It is not fair to make any deductions concerning the toxicity of sulfanilylguanidine in dogs which received 5 Gm. per kilo per day. It is significant, however, that several dogs survived this enormous dosage for 50 days—a fact which argues strongly for the relatively low toxicity. None of the original 12 surgical patients who received sulfanilylguanidine showed any signs of toxicity, but in the subsequent 36 patients four had mild toxic symptoms. Three of these four patients received the drug at four-hour intervals. The manifestations of toxicity were fever (four cases), erythematous rash (two cases), headache (two cases), anorexia and nausea (four cases), photophobia (one case), and conjunctivitis (one case). In every instance, the toxicity promptly disappeared upon the withdrawal of the medication. None of our patients developed hemolytic anemia, jaundice, hematuria, leukopenia, or granulocytopenia.

Apparently, the toxicity bears no relationship to the concentration of the

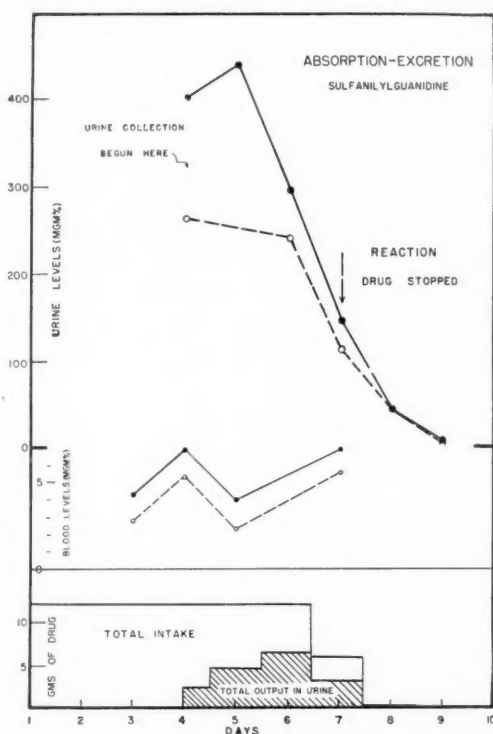


CHART 6.—The rates of absorption and excretion of sulfanilylguanidine by a patient with a normal gastrointestinal tract receiving two grams of the drug every four hours.

drug in the blood, but may be associated with the quantity of the drug absorbed and excreted. If 6 Gm. of the drug are excreted in 24 hours, and 40 per cent of the compound is conjugated, and the acetyl derivative has a solubility of 75 mg. per cent in urine, it would require an urinary output of 3,200 cc. to keep the acetyl derivative in solution, and thereby insure against the formation of crystals in the upper urinary tract.

It seems probable that toxic reactions of serious proportions can be avoided if certain precautions are followed. First, sulfanilylguanidine should not be given to patients with seriously impaired renal function. Second, the drug should be discontinued upon the first evidence of toxicity. Finally, the daily urinary output must be kept above 1,500 cc.

#### SUMMARY AND CONCLUSIONS

Experimental and clinical studies with sulfanilylguanidine have shown that when an adequate amount of the drug is given at sufficiently frequent intervals, the coliform flora of the bowel can usually be significantly reduced. This treatment does not decrease the number of other bacteria in the colon. No reduction in the number of coliform organisms has been obtained in the presence of ulcerative lesions of the bowel.

Although the drug is slowly absorbed when taken by mouth, a considerable quantity of the compound is absorbed under therapeutic conditions. Ordinarily, concentration in the blood remains low because the drug is rapidly eliminated in the urine. Abnormalities of absorption or excretion may cause a dangerous accumulation of the drug in the body.

Relatively mild toxic reactions have occurred in patients receiving sulfanilylguanidine by mouth. The more severe reactions caused by some of the other active sulfonamides have not occurred. Apparently, there is no relationship between the toxicity and the concentration of the drug in the blood. To avoid serious reactions, sulfanilylguanidine should not be given to patients with intestinal obstruction or with seriously impaired renal function, and should be withdrawn immediately upon the appearance of toxicity.

The authors thank Drs. F. Louis Knotts and Frank Inui for their assistance.

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DISCUSSION.—DR. HARVEY B. STONE (Baltimore, Md.): I shall limit my remarks to my own personal experience in the use of this drug: First, I would like to mention one

phase of its possible value which Doctor Firor did not touch upon in his paper. We have employed it in some six or eight cases of chronic ulcerative colitis, in the hope that it might prove of value in the treatment of this disease, and I regret to say that, so far as this scanty evidence goes, it proved to have no beneficial effect whatever, that we could recognize. It simply did nothing toward relieving the symptoms or improving the appearance of the mucous membrane in the bowel, as seen through the proctoscope.

I have used the drug as a preparatory measure in 25-odd cases in which the operation was planned upon the large bowel for one cause or another, and can report that in that series of cases there were no deaths as a result of the operation which followed this preparatory treatment. I think, however, that this is entirely negative evidence, because it is not at all unusual to run a series of 25 cases with the ordinary preoperative preparation, lacking sulfanilylguanidine, without a fatality, so that this evidence I think is of no great value.

In this group of cases, I had one patient who showed very much more severe toxic symptoms than those which Doctor Firor has reported in his experience. This patient ran a sudden elevation of temperature from a previous level of perhaps a maximum of 100° F. in the 24-hour chart, to an elevation of 103° F., with a pulse rate increasing from approximately 100 to 140, with coma, cyanosis, and had the general appearance of desperate illness. The drug was immediately stopped, and within 24 hours all of the symptoms completely disappeared, so that I think it is a fair assumption that this grave change in the patient's condition was actually a toxic manifestation of sulfanilylguanidine.

In conclusion, the evidence that I have so far acquired personally from the use of this drug has not been such as to lead me to think it has great value, and I have, personally, discontinued its employment as a preoperative preparatory measure for resections of the large bowel.

DR. HERMAN E. PEARSE, JR. (Rochester, N. Y.): I would like to ask Doctor Firor if he has used the drug in the treatment of regional ileitis or regional enteritis. We have, with a very slight experience, gained the impression that it may be valuable in at least controlling the symptoms in patients with this disorder who have extensive disease beyond the possibility of resection.

DR. WARFIELD M. FIROR (Baltimore, Md., closing): In answer to Doctor Pearse's question, I should say we have used sulfanilylguanidine in only one instance, with questionable benefit.

I think that I can quickly summarize our feeling about this compound: First, to gain any lowering in the concentration of the coliform bacilli in the stool, it is necessary to give the drug at four-hour intervals. Second, in the presence of ulcerative lesions, it seems to be ineffectual, and if this observation is generally confirmed it indicates a real limitation in the use of this compound.

We feel that the drug is absorbed in large quantities, but slowly, from the alimentary canal, and promptly excreted by the kidneys. Where there is a diseased bowel or impending or actual intestinal obstruction, the drug should not be employed. We believe that there will be an increasing number of reactions with the closer spacing of the doses.

Finally, I think we can summarize our feeling, as I did at the Southern Surgical Association, by saying that we do not think sulfanilylguanidine has great merit of its own, and that its chief value is that it points the way to a new approach for making surgery of the large bowel safer.

## THE SYNDROME OF MESENTERIC OR SUBPERITONEAL HEMORRHAGE (ABDOMINAL APOPLEXY)\*

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RUPTURE of intra-abdominal blood vessels in the absence of aneurysm or of direct major violence appears to be extremely rare. We have found but 18 reported cases, in only one of which (Crile and Newell) was the diagnosis made before operation or necropsy. We report three additional cases, bringing the total to 21; and in one of these there were two hemorrhages, two years apart—the only instance we have found of repeated, unconnected episodes of mesenteric apoplexy. From a study of these new cases and of the few previously reported, in sufficient detail, we believe it is possible to recognize a series of signs and symptoms, correlated with the progressive stages of such hemorrhages—a syndrome often sufficiently clear to permit clinical diagnosis.

### CLINICAL PICTURE

(1) *Age, Sex, and Vascular Condition.*—Mesenteric vascular rupture has occurred about twice as often in males as in females. The average age was 53, with only three patients under 40, the youngest 27. Arteriosclerosis, either demonstrated or presumed on account of age, was present in four-fifths of the cases, and well-marked hypertension in one-third.

(2) *Injury or Strain.*—These shortly preceded the onset of symptoms in each of our three patients, though in two the strain was relatively minor (being "jerked" when boarding a moving street car; carrying a heavy load of commuter's bundles on to a ferry). The patients were little impressed by these incidents, the histories being obtained only by persistent, direct questioning, and this may account for the fact that in only one of the previously reported cases was strain or injury recorded.

(3) *Character of Initial Pain.*—A fresh hematoma, confined between mesenteric leaves or spreading under visceral peritoneum, gives rise to the characteristic *dull, sickening pain* of peritoneum under tension. It is usually sudden in onset, persistent or gradually subsiding, rather than intermittent and colicky, as in obstruction, and is usually accompanied, sooner or later, by nausea and vomiting. Instead of the tense quiet of peritonitis, patients exhibit a restless and unsuccessful search for a position of comfort. Vomiting and evacuation of the bowel afford no relief.

(4) *Subsidence and Recurrence of Pain.*—If hemorrhage ceases, distress gradually subsides, only to return if the size of the hematoma is increased

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.



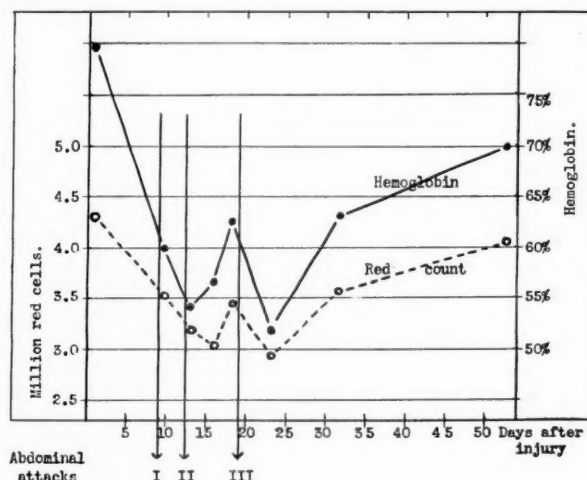
# ABDOMINAL APOPLEXY

by renewed bleeding. This *fading and return of pain* occurred in seven of the cases reported in the literature and in each of our three patients.

(5) *Secondary Severe Pain and Shock*.—With continued bleeding, rupture of a leaf of mesentery encapsulating the hematoma occurs and blood under tension is suddenly poured out into the peritoneal cavity. This produces *sudden, excruciating exacerbation of pain* followed rapidly by *collapse* with lowered blood pressure, clammy skin, rapid thready pulse and subnormal temperature.

Physical activity, vomiting, or the use of purgatives may increase or re-establish bleeding, and so be responsible for increase or recurrence of symptoms.

Time from initial pain to rupture into the abdominal cavity has varied from an interval too short to permit recognition of the symptoms of hematoma up to several days. In Silvertone's patient, the symptoms subsided after three days and returned two or three times before sudden collapse a week later. Bruce's patient had vague abdominal pains two days before his general peritoneal signs. Morton reported a clear example of repeated bleeding for a week before rupture of the hematoma. In our first case, onset occurred 24 hours before rupture into the abdominal cavity. There was temporary



CASE 5.  
Red counts and hemoglobin estimations.

CHART I.

subsidence of distress, exacerbation following eating, and again after taking castor oil. Rupture of the hematoma finally occurred during induced vomiting. Doubtless, subperitoneal hemorrhage has occurred in many instances without rupture into the general cavity, thus escaping operation and diagnosis.

(6) *Leukocytosis*.—The white count is usually elevated. In our cases, counts ranged from 11,600 and 12,700 with unruptured hematomata to 21,000, 24,000 and 26,000 with hemoperitoneum.

(7) *Red Count and Hemoglobin.*—If hemorrhage of considerable quantity occurs, ceases, and is renewed at long enough intervals to allow compensatory increase in blood volume, hemoglobin and red count will be reduced (see chart of Case 3).

*Treatment.*—In 17 patients operated upon, the source of bleeding was said to have been identified and ligated in seven, with but one death. Of ten cases in which no point of hemorrhage was located, four died. This suggests that operation is the treatment of choice. Yet it may well be that in some instances it was possible to identify and ligate bleeding vessels because of the fact that hematomata were less massive and extensive and that several of these patients might have recovered equally well without operation. Of the four instances (in three patients) reported here, recovery followed in two, without operation, and in two, after operation, at which nothing was done directly to stop bleeding.

If clinical diagnosis can be made, the duration and severity of symptoms may be a better guide to treatment than an invariable decision to operate upon all patients. If bleeding is slow or intermittent, expectant treatment with complete rest of the patient and his gastro-intestinal tract may well be indicated. If the period of time from onset to rupture of the hematoma is short, indicating rapid hemorrhage, prompt operation is obviously the treatment of choice.

#### CASE REPORTS

**Case 1.**—Male, age 40, steel worker. Shortly after dinner, this man ran a block or more and boarded a car after it had started. He received "quite a severe jerk" when he caught the hand rail but felt no abdominal pain at the moment. Ten or 15 minutes later, while sitting in a theater, dull pain began in his upper abdomen, constant, gradually increasing in severity. He felt an impulse to have a bowel movement, but a fairly large evacuation gave no relief. He left the theater and returned home because of increasing pain.

Discomfort was severe enough to keep him from sleeping that night but subsided toward morning. Immediately after eating a light breakfast, the same nagging, persistent pain in the epigastrium returned, and remained with moderate severity throughout the day while he rested at home. By evening it had lessened and he ate a fairly heavy dinner, followed by another exacerbation of distress. A large dose of castor oil served only to increase pain. By this time there was a little nausea. Vomiting was induced by gagging, during which the pain suddenly became agonizing throughout the entire upper abdomen and he felt as if a belt were being tightened about his waist.

One of us (G. F. C.) saw him about ten minutes later. He was moaning with pain, incessantly tossing about in bed, unable to find a position of even relative comfort. Pulse 120, thready and barely perceptible; blood pressure 70/50; skin clammy and cold; temperature 95.6° F. The abdomen was moderately tender throughout on deep pressure, but without rigidity or even localized muscle spasm. At hospital, an hour later, W.B.C. 26,000, 67 per cent polymorphonuclears. The patient was now vomiting small amounts of bile-stained fluid at frequent intervals, with no relief of exquisitely acute pain. *Tentative Diagnosis:* Mesenteric thrombosis.

*Operation.*—Upon opening the abdomen, under novocain, through an upper right rectus incision a large quantity of dark blood gushed out. The transverse mesocolon was distended by an hematoma between its leaves extending from root to colon and

from hepatic to splenic flexures. There was a rent in the lower surface of the mesocolon, through which blood had escaped; but the tear was filled with clot and no active bleeding could be found. The hemorrhage was presumably from a branch of the middle colic artery. There was no evidence of inadequate blood supply to the transverse colon. The abdomen was closed without drainage, and 100 cc. of whole blood injected intramuscularly.

Convalescence was uneventful. He was discharged from hospital in three weeks, and returned to work as a structural iron worker at the end of two months.

No cause for the hemorrhage could be determined, unless it was the seemingly insignificant injury of a "jerk" when boarding a moving street car. He had no appreciable thickening of peripheral arteries and blood pressure on several occasions was within normal range. Wassermann test was negative.

He remained well for two years. Then, about two hours after eating, without injury or strain, he suffered another attack of dull epigastric pain. It was not, at first, severe enough to prevent him from going to work but persisted and gradually increased in severity so that he had to quit and go home after a few hours. He described his pain as dull, "dragging" or "tearing" in character, constant and not intermittently cramping—the same, he said, as that in the attack two years before. A dose of castor oil was followed by vomiting, but this time no sudden major exacerbation of pain with shock and collapse followed.

The abdomen presented only a moderate degree of diffuse tenderness in its upper half. There was no muscle spasm and no mass was felt, either at first examination or later. Temperature 100° F.; pulse 94; W.B.C. 12,700, with 85 per cent polymorphonuclears; hemoglobin 95 per cent; R.B.C. 4,550,000. Intramuscular injection of whole blood was administered twice, and he was kept at rest and without food for 24 hours. Pain, fever, and leukocytosis subsided over a period of three days, and he was discharged with diagnosis of recurrence of mesenteric hemorrhage, not going on to rupture of the hematoma.

At recent physical examination, five years later, he was found in good health, having worked steadily and with no recurrence of abdominal distress.

**Case 2.**—Female, age 63, stenographer. She had had repeated attacks of epigastric pain over several years, diagnosed as cholecystitis but without jaundice or fever. She had had one attack of transitory vertigo a few months before present illness.

While carrying a considerable load of week-end supplies on to the ferry, she suddenly "felt as if something tore on each side, right from chest to abdomen." This pain lasted only a few seconds, she continued her trip, remained active and had no further distress during the rest of the day. In the afternoon of the following day, she began to have colicky pains across the lower abdomen, gradually increasing in intensity and finally becoming constant. An hour after the second onset she had nausea and then severe, repeated vomiting. The second morning she was still suffering pain and nausea. There was no fever; hemoglobin 94 per cent; R.B.C. 5,130,000; W.B.C. 11,600, 78 per cent polymorphonuclears; urine normal. Flat roentgenogram of the abdomen showed moderate distention of several loops of small intestine, suggesting at least partial obstruction.

At operation, in the evening of this second day of illness, a subperitoneal hemorrhage was found, extending from the base of a small, noninflamed Meckel's diverticulum eight inches toward the cecum, spreading under the peritoneum of the bowel rather than in the mesentery. The diverticulum was inverted with purse-string suture, though no active bleeding could be found. Recovery was uneventful.

This patient's peripheral vessels were not unusually hardened and her blood pressure was within normal limits. She died, however, five years after this incident from cerebral hemorrhage.

**Case 3.**—Male, age 51, bridgeworker. A rather heavily loaded supply car with steel-flanged wheels ran over his left thigh near the groin. He suffered an extensive

abrasion and contusion of the thigh, most severe on the mediodorsal aspect. The scrotum was contused and both testes swollen. The abdomen was soft, not tender, and presented no external evidence of injury. There was no fracture of pelvis or spine nor any bladder injury. Peripheral arteries were moderately thickened; blood pressure 125/60; W.B.C. 21,250, with 96 per cent polymorphonuclears; hemoglobin 80 per cent; R.B.C. 4,320,000.

His progress was satisfactory until the ninth day, when his temperature rose to 102.2° F. He complained of persistent, extremely annoying, dull ache about the umbilicus with a little nausea but no vomiting. On this day W.B.C. was 24,000; hemoglobin 60 per cent; R.B.C. 3,500,000.

The abdominal symptoms gradually subsided and he felt fairly well the following day. Two days later a similar episode occurred, subsiding this time in about 36 hours. White count during this attack was 19,200; hemoglobin 57 per cent; red count 3,040,000.

No further discomfort was complained of until another full week had elapsed. Red count had risen to 3,460,000, with hemoglobin 65 per cent. The third attack was identical in character with the two preceding ones—the same annoying, constant, aching pain centered around the umbilicus, associated with slight nausea. Repeated abdominal examinations demonstrated no tenderness, muscle spasm nor any mass. Hemoglobin after onset of the third attack dropped to 52 per cent; R.B.C. 2,900,000; W.B.C. 18,300.

The character of pain and its recurrence, associated with leukocytosis, afebrile except at first onset of pain, with such definite reduction in hemoglobin and red count (see chart) following each episode, led us to a diagnosis of subperitoneal hemorrhage, intermittently renewed but with hematoma unruptured into the general cavity. It was not until about one month later that a vaguely definable mass was first discovered in the right lower quadrant. It was about the size of a grapefruit, not tender and gave the impression of containing fluid. The patient had, by this time, no complaints that could be referred to it. Gastro-intestinal roentgenograms were reported as showing "a tumor mass in the right lower quadrant which does not invade the bowel but slightly displaces the cecum and terminal ileum."

The mass gradually diminished in size during the following two months while he was under observation. From its location, the hematoma presumably arose from a branch of the superior mesenteric artery. Although the first symptoms suggesting intra-abdominal hemorrhage did not appear until the ninth day following injury, it seems not improbable that the initial vascular rupture occurred at that time and that the more severe pain of the external injuries masked any abdominal distress. Each of the episodes of onset and subsidence of pain apparently represented transitory renewal of bleeding, which finally ceased without peritoneal rupture.

#### SUMMARY OF COLLECTED CASES

Available information about collected cases (including those herewith reported) is summarized in Table I.

Bleeding came from the distribution of the celiac axis in eight instances and the superior mesenteric in 12—source not identified in one.

In seven cases, the hematoma remained unruptured into the abdominal cavity, in the remainder, hemoperitoneum was found. In all but two of the latter, rupture of the hematoma gave rise to the characteristic clinical picture of profound collapse and shock. Roughly, about one-third began with pain and did not go on to collapse; about one-third began with pain, and after a period of several hours to several days, with or without intervening exacerbations, finally suffered rupture of hematoma into the abdominal cavity with

collapse; and in about one-third, peritoneal rupture occurred so early that collapse and shock were almost initial symptoms.

In this small group of cases, every patient age 50 or less (except our Case I, in his second attack) suffered rupture of the hematoma and hemoperitoneum.

Some degree of tenderness was usual, but muscle spasm appears to have varied from none at all to board-like rigidity whether or not hematomata had ruptured.

In the hematoma stage, a mass was felt in but two cases, and in one of these (our Case 3) not until three or four weeks after subsidence of symptoms.

Operation was performed for 17 of 22 hemorrhages (in 21 patients), with mortality of five (30 per cent); two were diagnosed clinically and recovered without operation (our Cases 1 and 3); three were diagnosed only at necropsy. Total mortality of the reported cases was, therefore, 37 per cent. However, some of the cases contributing to this high mortality were in advanced stages of cardiovascular disease, one or two already in hospital with hemiplegia or essential hypertension; and in some of these, the abdominal hemorrhage was doubtless only a terminal incident rather than a major factor in fatality.

#### SUMMARY

(1) Four new instances (in three patients) are added to 18 previously reported cases of mesenteric apoplexy.

(2) A clinical syndrome is described of signs and symptoms correlated with the progressive stages of hemorrhage: Usually in the presence of vascular deterioration, with or without injury or more or less strain or exertion, there occurs dull, "dragging," "pulling" or "tearing," often severe, persistent and increasing abdominal pain—the pain of peritoneal tension—later gradually subsiding but often recurring with renewal of hemorrhage, exacerbated by eating or by vomiting or catharsis; with leukocytosis and, if time permits, drop in red count and hemoglobin; and, finally, if the hematoma ruptures, sudden, severe pain, with shock and collapse.

(3) In two instances, we believe the clinical diagnosis was justified, although this was not confirmed because of recovery without operation.

(4) One patient suffered recurrence two years after the initial episode. This appears to be the first such case reported.

(5) Treatment is discussed, and it is suggested that decision for or against surgical intervention should depend upon the apparent rate of bleeding or the occurrence of early rupture into the abdominal cavity.

Since this paper was submitted, an additional case has been reported as intra-abdominal apoplexy, though no source of bleeding was demonstrated on extensive exploration (Berk, J. E., Rothschild, N. S., and Doane, J. C.: Intra-abdominal Apoplexy. *ANNALS OF SURGERY*, 113, 513-520, April, 1941).



TABLE  
SUMMARY OF

Author	Age	Sex	Etiologic Factors	Source of Bleeding	Duration of Symptoms	Number of Exacerbations After Onset	Collapse and Shock	Tenderness
Budde	27	M.		Left gastro-epiploic	6 hrs.		0	++
Florence and Ducuing	30	F.	In labor	Sup. mes.	48 hrs.	0		
Hartley and MacKechnie	31	M.		Sup. mes.	12 hrs.	1	0	0
Bruce	34	M.		Sup. mes.	48 hrs.	1	Secondary	+
G. F. C.-A. R. K., Case 1	40	M.	Mild trauma	Right colic	24 hrs.	4	Secondary	+
Same 2nd attack	42	M.	0	Same?	24 hrs.	0	0	+
Moorehead and McLester	44	M.	B. P. 220/140	Celiac axis	? (sudden death)		Initial	
Hilliard	48	M.	Hemiplegia hypertension	Sup. mes.	1 hr.	0	0	
Crile and Newell	49	F.	Essential hypertension	Middle colic	3 hrs.	0	Initial	+
Moorehead and McLester	50	M.	C.-V. Dis.	Sup. mes.	? (sudden death)		Initial	
G. F. C.-A. R. K., Case 3	51	M.	Trauma	Sup. mes.	2-3 weeks	3	0	0
Silverstone	52	M.	C.-V. dis.	?	1 week	5	Secondary	+++
Green and Powers	54	F.	B. P. 230	Left gastric	5 hrs.	0	0	++
Mourgue-Molines and Cabanac	56	M.	Arterio-sclerosis	Right gastric	? 48 hrs.	?1	? Secondary	0
Buchbinder and Greene	57	M.	Arterio-sclerosis B. P. 190	Right gastric	5 hrs.	0		++
Starcke	60	M.	Arterio-sclerosis	Gastro-duod.	2-3 days	1	Secondary	++
Thompson and Dunphy	62	F.	Hemiplegia hypertension	Celiac axis	18 hrs.	0	Initial	
G. F. C.-A. R. K., Case 2	63	F.	Arterio-sclerosis	Sup. mes.	2 days	1	0	++
Bruce	72	M.		Middle colic			Initial	++
Morton	72	M.		Sup. mes.	6 days	2	Secondary	
Mourgue-Molines and Cabanac	73	F.	Hemiplegia	Left gastro-epiploic	Few hrs.	0	0	
Cutler	80	F.	Arterio-sclerosis hypertension	Right colic	24 hrs.		Initial	+++

# ABDOMINAL APOPLEXY

## I

### COLLECTED CASES

Rigidity	White Count	Unrup- tured Hema- toma	Hemo- peri- toneum	Bleed- ing Vessel Lig- ated	Bleed- ing Vessel Not Found	Not Oper- ated	Recov- ered	Died	
+++			+	+			+		
+++			+			+		+	Autopsy diagno- sis. Gangrene of bowel
+			+		+			+	
+	26,150		+		+		+		
o	12,700	+				+	+		
			+			+		+	Autopsy diagno- sis
+++			+		+			+	
+			+	Bowel resected			+		Mass felt
			+			+		+	Autopsy diagno- sis
o	26,000	+				+	+		Mass felt late
o			+		+			+	
+++	20,000	+		+			+		
o			+	Packed	+		+		
+++	8,500	+		+			+		
+++			+	+			+		
	18,700		+	+			+		
o	11,700	+			+		+		
o			+		+			+	
		+	+	+	+		+	+	
++		+			+		+		

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DISCUSSION.—DR. RICHARD H. MILLER (Boston): This very informative presentation serves to call our attention to a condition which I think can hardly be as rare as Doctor Kilgore has stated. I believe cases have occurred more frequently, but they have failed to arouse the interest of the profession enough to lead them to record them in the literature. It is extraordinary, when you come to think of it, that only about 20 cases have been noted.

The syndrome which Doctors Kilgore and Cushman have noted is indeed worthy of our consideration, and we ought to bear it in mind whenever we are called in to study a doubtful acute abdominal case. Their third patient was one in whom they did not definitely prove the diagnosis by operation, and one, on reading the paper, is tempted to say: "Well, perhaps it might have been something else." But on further study, one is convinced, from one's own reasoning, that that is what truly obtained, and one can but commend them for making the diagnosis and, once having made it, for adhering to it and carrying out a policy of conservative treatment, when it would have been perfectly justifiable, and easier, to have performed an exploratory operation.

When you group all these cases together and study them, it is at once evident that the picture is not entirely a clear-cut one, because several of these patients did not show evidence of any vascular disease, and it is difficult, in view of their comparative youth, to explain the etiologic factors involved. I think it is important that such cases, as may be met, be reported and studied more carefully in the future.

There are two cases which I will mention, with the greatest brevity. The first is one that we had in the Massachusetts General Hospital not long ago, operated upon by Dr. Arthur Allen. A woman, age 59, with a normal blood pressure, who, following a bad cold accompanied by severe coughing, began to have pain in the left lower quadrant of the abdomen. A careful study failed to reveal the exact diagnosis. The pain was

## ABDOMINAL APOPLEXY

characteristic of that of smooth muscle contraction, not of peritonitis. She was finally operated upon, and as soon as the anesthetic was administered, it became obvious that a vague mass, which had previously been felt in the abdomen, was in the abdominal wall, and the lesion proved to be a spontaneous rupture of the deep left epigastric artery, with a large hematoma.

The other case is one which is not positively proved, but is extremely interesting, and I believe to have been an instance of this condition. A man, age 45, with a systolic blood pressure of 250, was operated upon by myself, at his request, for hernia. The operation was uneventful, and there was no trouble until five weeks postoperative, when he was seized with a vague attack of acute abdominal pain, with nausea and vomiting, but no obstruction, no definite tenderness, and no palpable tumor. He continued to have symptoms for seven days, during five of which he passed frequent stools containing blood which was partially changed, neither tarry nor bright red, but of a purple tinge. There was considerable argument as to whether he should be operated upon again, the feeling being that probably he had a very small mesenteric thrombosis.

He recovered without operation. His condition of arteriosclerosis became progressively worse, and at the end of six months he died. Autopsy revealed, about half-way up the ileum, the scar of a recent ulcer surrounded by scar tissue, and it is my belief that he had what was not a mesenteric thrombosis, but a rupture of an artery, with the formation of a small hematoma, interference with the circulation, ulceration of the mucous membrane of the ileum, and hemorrhage.

DR. DALLAS R. PHEMISTER (Chicago): I only wish to point out that in hemorrhagic pancreatitis there may be not only an hematoma about the pancreas but an enormous hematoma extending down into the mesentery, producing precisely the clinical picture cited by Doctor Kilgore.

## EXPERIMENTAL PRODUCTION OF CHRONIC CHOLECYSTITIS BY OBSTRUCTIVE LESIONS OF THE CYSTIC DUCT\*

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It has long been known that complete obstruction of the cystic duct results in definite pathologic changes such as hydrops and empyema, which are associated with a variable degree of inflammation of the wall of the gallbladder and give rise to certain symptoms. It has not been conceded that partial obstruction of the cystic duct would result in definite pathologic changes or symptoms. However, as long ago as 1921, Schmieden and Rhode,<sup>1</sup> and Seelig<sup>2</sup> called attention to this possibility. Little has been done since then to foster the idea. In 1938, Cole and Rossiter<sup>3</sup> called attention again to the possible relationship of obstructive lesions of the cystic duct to inflammation of the gallbladder. This work was instigated by the observation of the high incidence of obstructive lesions in the cystic duct of gallbladders removed in the operating room.

In support of the assumption that partial obstruction of the cystic duct exists and may result in pathologic changes, one might mention the fact that partial obstruction in practically all tubular structures of the body including intestines, ureter, urethra, bronchus, *etc.*, almost always leads to symptoms or pathologic lesions, or both. Since the function of the cystic duct is to conduct bile from the common duct to the gallbladder, why should not an obstruction here be fairly common and likewise produce a pathologic condition?

Although various types of obstructive lesions of the cystic duct including anomalous valves of Heister, stenosis, kinking, *etc.*, are found, it is somewhat difficult to determine the exact importance of these lesions, chiefly because it is frequently difficult to tell how much obstruction is produced by a given lesion. However, careful examination of the cystic duct of gallbladders removed for cholecystitis will show remarkably few normal ducts, particularly if the duct has been removed close to the common duct.

The incidence of anomalies in this area is well exemplified by the study of Flint,<sup>4</sup> who noted that in 200 cadavers an anomalous condition of the cystic artery, bile ducts, hepatic artery, and gastroduodenal artery existed in 65 per cent of the cases. In a study of 194 cadavers, Lurje<sup>5</sup> found an anomalous arrangement of cystic duct alone in 53 per cent of specimens examined. These two studies contain observations only on the anatomic position of the structures, and make no mention of anomalies inside the duct;

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yet it seems likely that a large proportion of the lesions described by them would result in partial obstruction.

By producing obstructive lesions of the cystic duct, after methods to be described presently, we obtained changes in the gallbladder identical to chronic cholecystitis in the human, in practically 100 per cent of the cases. These changes, however, were minimal for three or four months, and did not become marked until eight or ten months had passed since production of the obstruction. Although we did not conduct experiments to explain the mechanism of the production of the lesion, certain possibilities seem apparent. We initially tried to produce a lesion which might have a valvular action, thereby allowing bile to enter the cystic duct more readily than get out. We found, however, that the lesion in the fundus was produced regardless of whether or not the obstructive lesion was of such a nature as to produce a valvular action. Concentration of the bile in the gallbladder (seven or eight times under normal circumstances) results in a definite increase in viscosity. Since the lumen of the cystic duct already is relatively small for the transmission of a viscid fluid, the increase in viscosity would obviously exert a rather marked influence in retardation of the exit of the bile into the common duct. It seems logical to us that this chronic partial obstruction would result in an overconcentration of bile, thereby exposing the mucous membrane to a fluid which might be damaging to it.

This theory of chemical cholecystitis is not as yet generally accepted, but is rapidly gaining momentum. It was originated several years ago by Denton<sup>6</sup> and Feinblatt.<sup>7</sup> One of the features impressing Feinblatt with the fallacy of infection as the primary lesion was the fact that in 20 cases of empyema of the gallbladder he found the contents to consist for the most part of cholesterol and débris, and yielded a positive culture in only 40 per cent of the cases. This idea has been promoted to a greater extent by Andrews and associates.<sup>8</sup> They noted that if bile, concentrated to no more than one-half its volume, were injected into a dog's gallbladder a severe cholecystitis invariably resulted, and concluded that the changes obtained were primarily chemical. These changes have been reproduced by Womack and Bricker,<sup>9</sup> who concluded that the pathologic lesion resulting from exposure of the gallbladder mucosa to a bile concentrated no more than twice normal, was identical to chronic cholecystitis of human beings. This idea is being accepted by more and more investigators, and is the basic factor behind the fact that cholecystectomy can be performed for acute cholecystitis with only rare development of peritonitis and with a very low mortality rate.

The relatively low incidence of positive cultures of bile and gallbladder wall from gallbladders removed at operation cannot be considered data supporting the infectious etiology of cholecystitis in the human being, at least not in all instances. Judd and associates<sup>10</sup> found a positive culture in the bile in 14 per cent of cases of cholecystitis, and a positive culture in the gallbladder wall in 49 per cent. These figures represent a fair average of the various reports available. In a summary of reports assembled by Walters

and Snell,<sup>11</sup> streptococci and *B. coli* were found with about the same frequency. In acute cholecystitis, the percentage of positive cultures will be slightly higher.

Although these experiments were not concerned with the production of gallstones, we found stones in the gallbladder of one animal, and huge deposits of soft tarry material in the gallbladder of another animal, both of which had had a partial obstruction of the cystic duct for about two years. The experimental work of Phemister and associates,<sup>12</sup> showing that the deposition of calcium as stones, or on stones in the gallbladder is dependent upon the degree of obstruction of the cystic duct, supports to a certain extent our theory that partial obstruction will produce pathologic changes. The relationship between complete obstruction of the cystic duct (by stone) and cholecystitis has been discussed adequately by these authors and need not be cited here.

The most obvious explanation of production of chronic cholecystitis by chronic obstruction of the cystic duct as noted in our experiments, would appear to lie in the production of a chemical cholecystitis (similar to that described above) followed later by a superimposed infection in many cases. This hypothesis does not conflict with the method of infection by lymphatic channels as brought out by Graham<sup>13</sup> many years ago. In fact, it is our assumption that in our animals, the infection, as found in 30 per cent of chronically inflamed gallbladders, took place by such a mechanism. That principle is, therefore, needed to explain part of the findings in our work.

*Methods of Experimentation.*—Three different methods of producing a partial obstruction of the cystic duct were utilized: (1) A small flap of gallbladder wall was outlined in the neck of the gallbladder (Fig. 1), the flap turned into the lumen of the organ and the opening closed. We thought this flap might remain as a mobile piece of gallbladder wall obstructing the cystic duct because of its position directly over the opening. However, we discovered that as the lesion healed the flap became rounded and developed into a pear-shaped nodule (Fig. 1). If the flap were made in the proper position at the junction of the neck of the gallbladder and opening of the cystic duct, it would protrude against the opposite wall of the neck of the gallbladder producing an obvious partial obstruction of the valvular type because of its position on the gallbladder side of the cystic duct. After two or three trials we found it was not difficult to place this flap at the proper position. Control flaps were made in the dome of several dogs to eliminate the possibility that simple incision through the gallbladder wall might produce a lesion which would spread throughout the entire gallbladder. We noted a definite thickening of the gallbladder wall surrounding the site of the control flap in the dome, but in no instance did this fibrous tissue extend further than 1 or 1.5 cm. beyond the operative site.\*

\* Attention is called to the universal temporary diffuse reaction consisting primarily of edema in the wall following even trivial injuries of the gallbladder wall; however, this injury in our experience heals without residue if inflicted in the dome of the gallbladder.

## CHRONIC CHOLECYSTITIS

(2) Partial obstruction of the cystic duct was also produced by taking three or four interrupted mattress sutures of silk in the neck of the gallbladder at the margin of the cystic duct, thereby infolding the wall against the opposite side. This procedure amounts to taking a tuck in the wall, and produced a partial obstruction in three of the four animals upon which the procedure was performed.

(3) The cystic duct was crushed in seven animals; thinking that when healing took place a stenosis would result. In spite of the fact that the crushing was thought to have been thorough we noted, to our amazement, that the injury healed in about half of the animals without any obvious residual lesion. This method was, therefore, considered unreliable, at least in our hands, for the production of an obstruction. Perhaps the crushing was not sufficiently complete.

*Results of Experiments.*—All together, 36 animals were used. Two of these died a few days postoperatively, and two represent errors in technic, insofar as our attempt to produce a partial obstruction actually resulted in a total obstruction. These animals with total obstruction of the cystic duct showed a small shriveled gallbladder, as observed at a later date, containing no bile, but naturally showed evidence of inflammation. These four animals, therefore, had to be discarded.

Of the remaining 32 animals, nine had the operation consisting of production of a flap in the neck of the gallbladder at the junction with the cystic duct. These dogs were sacrificed at various intervals ranging from two to 24 months following the operation (Table I). One animal was sacrificed at two months, and practically all the remaining had operations at three months (but were not killed) to observe any gross changes present. None of the animals in any series showed any gross change (except edema) at operation or at autopsy, when the obstruction was produced less than four months previously. On several occasions, when observations were obtained a few days or a few weeks following operation, edema was noted, regardless of the type of operation, as previously discussed. Of the nine animals having flaps produced at the neck of the gallbladder, one was sacrificed at two months, too early for development of change, and thereby actually served as a control. Table I reveals that of the remaining eight, all except one

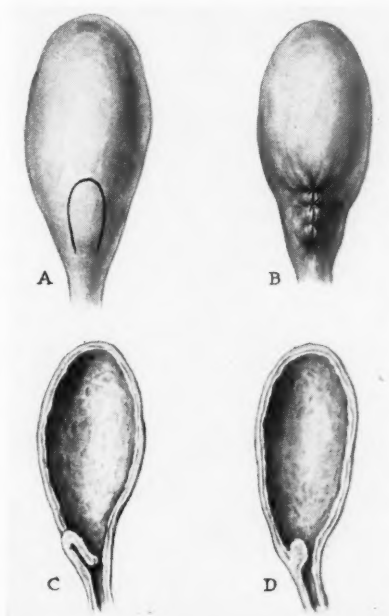


FIG. 1.—The most effective of the three methods tried for production of partial obstruction of the cystic duct. A. A flap is outlined in the neck of the gallbladder, and is turned in with closure of the defect as shown in B and C. Usually the flap becomes rounded as depicted in D, but frequently disappears, leaving a densely scarred area with obstruction at the proximal opening of the duct.

TABLE I

	Dog No.	Dur. Obst., Mo.	Gross Change	Culture	Thickness (Times Normal)	Obst. Prod. in Cyst. Duct	Remarks
Flap at neck of G.B.	1	24	++++	An. strep.	5.5 X	Yes	
	2	24	++++	Neg.	4.5 X	Yes	Stone at cystic duct
	3	19	+++	Staph. & strep.	4 X	Yes	
	4	15	0 to +	Neg.	-2 X	No	No evidence flap or oper.
	5	8	++		2 X	Yes	
	6	7	++	An. strep.	4 X	Yes	Flap gone; stricture
	7	7	+++	Neg.	3 X	Yes	
	8	6	++	Neg.	2.8 X	Yes	Soft stones?
	9	2	+		1.5 X	Yes	Too early for change
Tuck at neck of G.B.	10	12	+++	Neg.	5 X	Yes	
	11	11	+	Neg.	2 X	?	
	12	7	+++		3 X	Yes	
	13	4	+	Neg.	2 X	?	Insuf. time
Crush cystic duct	14	17	++++	Neg.	4 X	Yes	Stricture
	15	15	0	Neg.	1.4 X	No	
	16	12	0	Contam.?	1.0 X	No	
	17	7	+++	Neg.	2.5 X	Yes	Stricture; cholesterosis
	18	7	+++	Neg.	3.5 X	Yes	Stricture
	19	7	0	Neg.	1 X	No	
	20	0.3	+(Edema)		2 X	?	Too early for change
Ligate cystic artery (No. obst.)	21	19	0		1 X	No	
	22	16	0	Neg.	1 X	No	
	23	8	0	Neg.	1 X	No	
	24	7	0		1 X	No	
	25	5	0		1 X	No	
	26	4	0		1 X	No	
Control: Flap midway	27	11	0 to +	Neg.	1.5 X	No	
Control: Flap in dome	28	11	0	Neg.	1 X	No	
	29	9	0		1 X	No	
	30	9	0		1 X	No	
	31	8	0	Neg.	1 X	No	
	32	4	0	Neg.	1 X	No	

Note that chronic cholecystitis was produced only in the animals in which an obstruction of the cystic duct was produced; chronic cholecystitis was produced in every gallbladder when the cystic duct was obstructed. The procedure of turning in a flap of gallbladder wall at the neck of the gallbladder was the most effective.

showed marked change of the type similar or identical to chronic cholecystitis as seen in human beings. The maximum thickness of the gallbladder, as measured microscopically on the sections, was 5.5 times normal. The average thickness of the eight gallbladders was slightly less than three and one-half times normal. It should be stated that the sections removed for microscopic study were removed from the fundus, as far as possible from the operative site. At postmortem, the gallbladder, in all instances except one (when no obstruction was produced), had lost its bluish color, presented a grayish-brick-red color, and had an obvious thickening of the wall. There were numerous adhesions of the omentum to the gallbladder in almost all cases. One of the eight gallbladders contained definite, firm stones. An additional one contained thick desiccated bile which was lumpy, indicating that stone formation was beginning. This animal had had an obstruction produced only

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six months previously, suggesting that an additional length of time might have shown more definite stone formation.

The microscopic change consisted primarily of fibrosis affecting the wall of the gallbladder. This fibrosis was located primarily in the muscularis and in the areolar tissue between the muscularis and serosa. Edema was found on numerous occasions regardless of the length of time since production of the obstruction. There was an infiltration of lymphocytes in all gallbladders showing significant change. This infiltration was diffuse but most marked in the submucosa. On numerous occasions the mucosa was gone. Realizing that the gallbladder mucosa can readily be lost during the process of fixation and staining, not a great deal of importance can be attached to this feature. However, it is significant that there was no loss of mucosa in any of the gallbladders showing no gross pathologic change. It is noted, therefore,

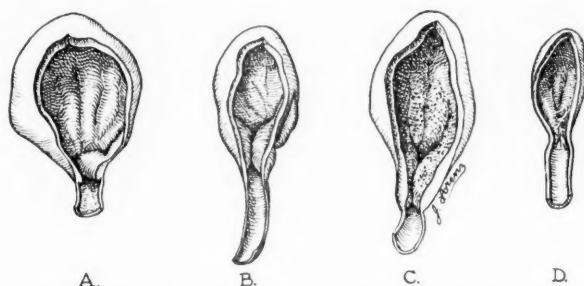


FIG. 2.—Drawings of four types of obstructive lesions produced in the cystic duct. A. and B. Produced by turning in a flap at the junction of the cystic duct and neck of the gallbladder, 7 and 10 months previously, respectively. C. Produced by infolding the wall of the gallbladder just above the cystic duct, 12 months previously. D. Produced by crushing the neck of the gallbladder and cystic duct, 17 months previously.

that seven of the eight gallbladders in this series showed very definite and pronounced evidence of chronic cholecystitis. The case showing no cholecystitis (Dog No. 4) revealed no evidence of obstruction at the junction of the cystic duct where the operation had supposedly been performed; neither was there any stenosis. In view of the fact that we could not find any changes at the operative site, the question was even raised as to whether or not there was an error in numbering the animals. We, however, classified this as an operative failure, but it does not influence the incidence of chronic cholecystitis in animals with partial obstruction of the cystic duct produced by this method, since all seven animals with obstruction of the duct showed a definite and fairly severe grade of chronic cholecystitis.

In four animals, an obstruction was produced at the junction of the cystic duct and neck of the gallbladder by taking a tuck at that point. This tuck, which was produced by mattress sutures, obviously resulted in an infolding of the wall into the lumen just above the cystic duct. Of these four animals (Table I), only two demonstrated definite pathologic changes. The other two showed only very slight pathologic change; examination of



the duct revealed that only a very slight ridge or infolding of tissue remained. One of these animals was sacrificed at the end of four months, but in view of the mild or doubtful obstruction produced, we would not expect much increase in the pathologic change even though many more months had elapsed.

In seven animals, the cystic duct was crushed at several areas with an artery forcep. Examination of the cystic duct revealed the fact that in only three animals was a stenosis produced by the crushing; in only these three was a definite cholecystitis produced. One of these gallbladders was the seat of a marked cholesterosis. One of the remaining four animals (Dog No. 20) was killed in a fight on his ninth postoperative day. As expected, the gallbladder wall showed edema and was moderately thickened, but the animal must be discarded because of inadequate time-interval since operation. In other words, this procedure resulted in positive results in only one-half of the cases, primarily because with the type of crushing performed we were unable to produce a stenosis or obstruction of any type, in half the cases.

In six animals, the cystic artery along with adjacent lymphatic ducts was ligated, to determine whether or not obstruction of the blood supply with adjacent lymph vessels would produce cholecystitis. In none of the six animals was there the slightest change noted in the gallbladder wall. The time interval since operation varied from four to 19 months (Table I). It should be stated, however, that this procedure will result in production of a significant edema several days after operation, but this edema disappears in several days or a few weeks leaving a normal gallbladder wall.

One animal (Dog No. 27) had a flap turned in at the junction of the middle and lower third of the gallbladder. This animal really serves as a control since no obstruction was produced. No changes other than those which might be secondary to a celiotomy were noted in this animal.

In five animals, control flaps were made in the dome of the gallbladder. The time-interval since operation varied from four to 11 months. In no instance was there any gross change or thickness of the gallbladder wall, except at the exact site of the operation, as noted at microscopic examination. These animals serve as controls, particularly for the ones having a flap turned in at the neck of the gallbladder.

Cultures were taken on the gallbladders of 22 animals. In ten of these animals, a definite obstruction had been produced with resultant pathologic changes in the gallbladder wall identical to chronic cholecystitis in the human being. The culture was positive in three instances, resulting in positive cultures in 30 per cent of the cases showing cholecystitis. All three of these positive cultures were obtained in the animals having had an obstruction produced by turning in a flap just above the cystic duct, thereby supporting the information already obtained that obstruction produced by a flap at the cystic duct was the most effective of the three methods tried. In two instances (Dogs Nos. 1 and 5) anaerobic streptococci were isolated from the gallbladder wall and bile. In one of these it was an *alpha* hemolytic streptococcus and in the other a *beta* hemolytic streptococcus. In Dog No. 3 a

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*Staphylococcus albus* and an *alpha* streptococcus were isolated from the gallbladder wall and the bile. The staphylococcus was present as a heavy growth (12,000 per cc. of bile), and the streptococcus almost as heavy

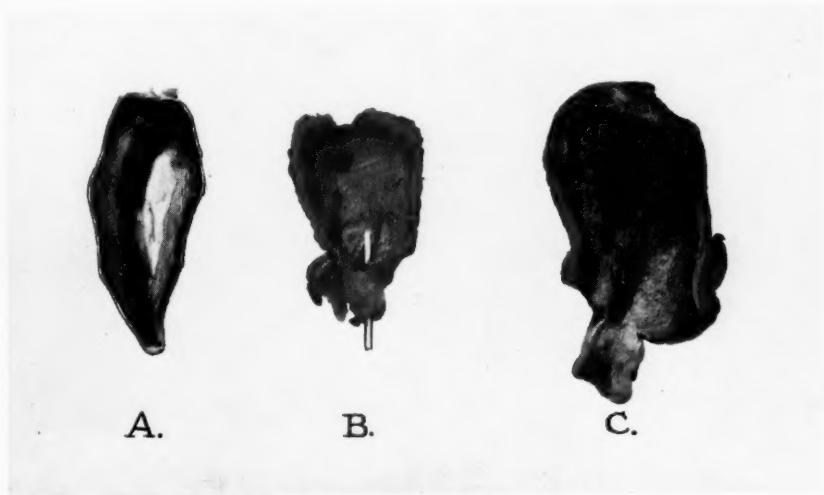


FIG. 3.—Photograph of three gallbladders. A. Control: Flap made in dome, 11 months previously. No gross or microscopic change noted except at the operative site (Fig. 4). B. Partial obstruction of cystic duct produced by inversion of a flap at the neck of the gallbladder 24 months previously. The small probe in the cystic duct reveals how the irregularly shaped nodule at the site of the flap compresses the opening of the duct. Note thickness of gallbladder wall as compared to the control. C. Partial obstruction produced by flap turned in at the neck of the gallbladder, 24 months previously. The flap disappeared, but a diffuse scar with severe contraction and consequent obstruction remained. Note the thickening of the gallbladder wall, a photomicrograph of which is shown in Figure 6.

(10,800 per cc. of bile). On one other occasion (Dog No. 16) a few staphylococci were found, but were considered to be contamination. This incidence of 30 per cent positive cultures in the bile and wall of the gallbladders in which chronic cholecystitis was produced, compares favorably with the incidence of positive cultures in chronic cholecystitis in the human being. It seems particularly significant that in all gallbladders without obstruction in which cultures were taken (12 in number), all were negative. Of these 12, five were controls.

COMMENT.—It is well known that operative procedures on the gallbladder, even though of minimal degree, result in subacute cholecystitis in a remarkably high percentage of cases. Edema is the important pathologic manifestation of this process. However, this temporary inflammation apparently disappears in several days or a few weeks. We encountered it in some of our cases a few days following operation, but when the animal was sacrificed months later no evidence of cholecystitis remained except when obstruction incident to our operative procedures existed. We resorted to three methods of producing obstruction at the cystic duct: (1) Flap in the neck of the gallbladder overlying the entrance to the cystic duct; (2) infolding of the neck of the gallbladder (tuck); (3) crushing of the cystic duct with the hope that a stenosis would be produced. In every gallbladder, in which

a definite obstruction of the cystic duct was produced (12 in number), a pronounced cholecystitis with thickening of the wall by fibrosis, and lymphocytic infiltration was observed. Of the three methods utilized for producing an obstruction of the cystic duct, the first one named (flap at neck) was the



FIG. 4.—Low power photomicrograph of control gallbladder (same as Fig. 3A), in which a flap was turned in on the dome, 11 months previously; no obstruction was produced at the cystic duct. There are no pathologic microscopic changes. ( $\times 65$ )

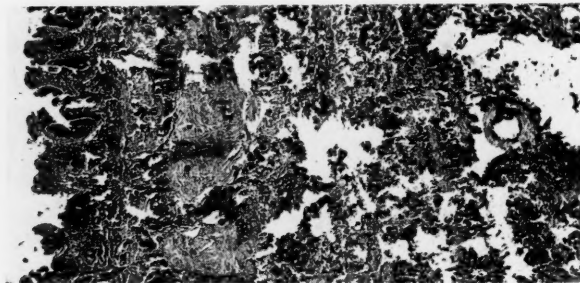


FIG. 5.—Low power photomicrograph of dome of gallbladder in which a flap was turned in at the neck, 24 months previously, producing a partial obstruction of the cystic duct. According to measurements made on the slides microscopically, the wall was five and one-half times thicker than the control illustrated in Figure 4. A dense deposition of fibrous tissue may be noted in the submucosa and muscularis. The tissue external to this represents edematous granulation tissue in various stages of resolution. Lymphocytic infiltration is diffuse, but polymorphonuclear cells are uncommon. ( $\times 65$ )

most effective, failing to produce an obstruction in only one instance (88 per cent successful). The second and third methods just described were successful in producing obstruction in 50 and 43 per cent, respectively. As stated, without exception the failures in production of cholecystitis occurred in the gallbladders in which the operative procedure failed to produce an obstruction at the opening of the cystic duct.

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To prove that disturbance of the blood supply, as would result from our operative procedures at the neck of the gallbladder, was not responsible for the cholecystitis, we ligated the cystic artery and adjacent lymphatic ducts in six animals. Although a temporary edema with gross thickening of the wall of the gallbladder results from such a procedure, complete recovery takes

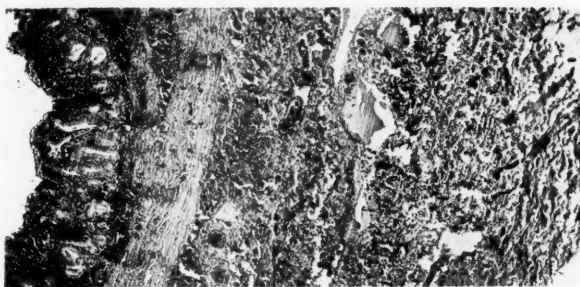


FIG. 6.—Low power photomicrograph of dome of gallbladder. A flap was turned in at the junction of the cystic duct and neck of the gallbladder, 24 months previously, resulting in a stenosis of the cystic duct (same gallbladder as in Fig. 3C). Chronic cholecystitis was produced. The wall is four and one-half times as thick as the control shown in Figure 4. The microscopic changes are the same as in Figure 5; however, two stones were found in the gallbladder lumen. ( $\times 65$ )

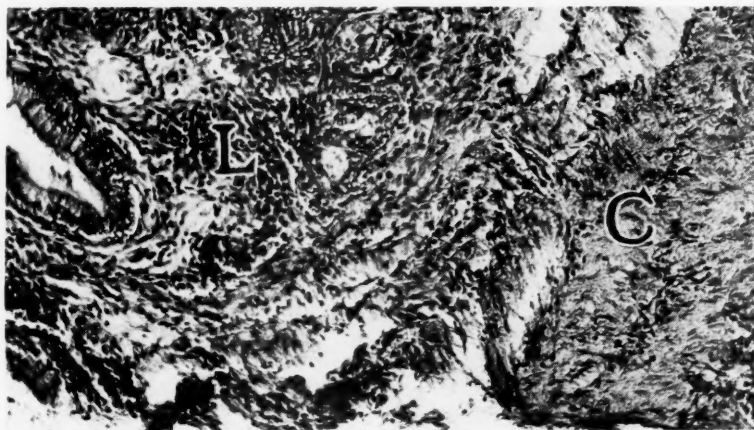


FIG. 7.—Moderately high power of gallbladder wall shown in Figure 6. The field depicted is between the muscularis and submucosa. Note the area of lymphocytic infiltration (L) near the mucosa, and the dense connective tissue (C) deeper in the wall. The microscopic picture is identical to that seen in a severe grade of chronic cholecystitis in the human being.

place; when these animals were sacrificed at intervals of four to 19 months following operation (Table I), not a single one exhibited evidence of cholecystitis. Moreover, control flaps were made in the dome of the gallbladder in five animals. In none of these was there evidence of cholecystitis at the time they were sacrificed, between four and 11 months following operation. It is obvious, then, that production of an obstruction at the neck of the gallbladder at the entrance of the cystic duct is the primary factor in the produc-

tion of the cholecystitis obtained. As noted in Figure 1, the flap changes markedly in shape; it usually becomes pear-shaped and consists entirely of a fibrous nodule, which projects inward over the opening of the cystic duct. Such a lesion would appear to interfere more with emptying of the organ than with its filling. The degree of cholecystitis produced was only slightly more pronounced than in gallbladders in which obstruction to the duct had been produced by other means.

As previously intimated, it is our assumption that this chronic inflammation is produced by exposure of the gallbladder mucosa to bile which is overly concentrated because of the chronic obstruction at the cystic duct. Attention has already been called to the fact that injection of gallbladder bile concentrated to twice normal (Andrews, Womack, and Bricker) will produce an acute cholecystitis, sometimes gangrenous in type. Presumably, the concentration in a partially obstructed gallbladder does not approach twice normal concentration; otherwise, we would have encountered acute cholecystitis perhaps with gangrene. It would appear that exposure of the gallbladder lumen over a period of months, to a bile concentrated slightly beyond normal might result in a chronic inflammation.

The incidence of positive cultures in the gallbladders with partial obstruction of the cystic duct showing cholecystic changes was 30 per cent. This corresponds closely with the incidence of positive cultures obtained in the wall of infected gallbladders of human beings. It is our contention that the organisms found in these specimens represented a secondary infection implanted on a chemical cholecystitis.

TABLE II

LESIONS WHICH MAY BE RESPONSIBLE FOR PARTIAL OBSTRUCTION  
OF THE CYSTIC DUCT\*

- (1) Congenital or inflammatory lesions involving valves of Heister.
  - (a) Valve-like anomalies.
  - (b) Fibrous strands.
  - (c) Local deposition (nodules) of fibrous tissue.
  - (d) Stricture due to scar.
- (2) Congenital or inflammatory twists or kinks.
- (3) Stenosis produced by a thickened wall.
  - (a) Due to acute inflammation.
  - (b) Due to diffuse fibrosis.
- (4) Stenosis produced by surrounding adhesions.
- (5) Stone in the duct.
- (6) Tension induced by enlarged liver.
- (7) Compression or filling defect due to tumor or lymph nodes.
- (8) Obstruction due to anomalous hepatic or cystic artery.

\* The authors are of the opinion that the first four types of obstruction would be the most important (from the standpoint of frequency) in the production of chronic cholecystitis by the mechanism herein suggested.

We do not infer that this mechanism of production of cholecystitis by partial obstruction of the cystic duct takes place in every instance of cholecystitis. However, the ease with which it is produced in animals, and the frequency of anomalous obstructive lesions in the cystic duct of gallbladders removed at operation, lead us to believe that it is a very frequent mechanism



in the production of chronic cholecystitis. In a study of incidence of obstructive lesions of the cystic duct in humans (not yet published) Jensik<sup>14</sup> has found them much more frequent in diseased gallbladders removed at operation than in normal gallbladders as removed at autopsy.

As previously stated, this hypothesis does not contradict the infective theory of lymphatic transmission as suggested by Graham many years ago. In fact, the infective theory is necessary to explain part of the findings in our experiments, insofar as the infection (positive culture) found in 30 per cent of the gallbladders with cholecystitis, in our experiments, was most likely explained by transmission from the liver through the lymphatics.

The fact that obstruction of the common duct by a lesion such as carcinoma of the pancreas does not give rise to cholecystitis, would at first appear to contradict the theory of origin of cholecystitis from partial obstruction of the cystic duct, as herein discussed. However, this apparent discrepancy can be explained readily. It has long been known and proved that almost immediately after an obstruction of the common duct is produced, the excretion of bile salts by the liver decreases to very low values. In that case, there would not be sufficient bile salts in the biliary tree to result in over-concentration in the gallbladder; chemical damage to the gallbladder wall from that source would, therefore, be impossible. The fact that obstruction of the common duct by lesions such as carcinoma of the pancreas does not instigate the development of cholecystitis, in reality, then supports the theory of origin from partial obstruction of the cystic duct.

Another peculiar feature of gallbladder disease, which might appear to be inconsistent with the theory herein presented, is the fact that cholecystitis is, in reality, a disease of adults. The question might be asked—if partial obstruction of the cystic duct such as produced by kinks, anomalous valves, *etc.*, are important in the pathogenesis of cholecystitis, why should the disease not be more common in childhood, since many of the obstructive lesions mentioned are congenital in origin? This question might be answered in many ways. In the first place, there are innumerable diseases which are much more common in late adult life than in childhood, when the etiologic factors *presumably* exist to the same extent in childhood as in late adult life. Among these may be mentioned cholelithiasis, arteriosclerosis, hepatic cirrhosis, carcinoma, and many others. The truth is that there, obviously, are reasons (chiefly physiologic) in all instances for the variation in incidence of cholecystitis in the various age-groups. An important reason for the infrequency of chronic cholecystitis in childhood may be contained in the possibility that there may be sufficient differences in the ratio of one bile salt to another in children, *versus* that in adults, to account for a different chemical action. After all, bile salts may not be the all-important factor in the production of chemical cholecystitis; the toxic action may be due to an allied salt, minute in quantity, which is not present normally until late in life. Perhaps the mucosa of the gallbladder in children is more resistant to injury or more impermeable to bile salts.

Another explanation may lie in the fact that although many lesions exist at birth they do not become obstructive to a damaging degree until they are actually increased in mass by the numerous assaults, from the wear and tear of time, which might gradually increase the amount of fibrous tissue and, therefore, the size. Anatomically, the tissue about the common duct and terminal end of the cystic duct contains many lymphatic channels communicating between the liver and celiac lymph nodes, and, perhaps, some draining directly from the intestine. It is well known that the liver is at all times being exposed to organisms brought to it from the intestinal tract by the portal vein. At frequent intervals, during attacks of hepatitis of bacterial origin some organisms no doubt spill over into the lymph ducts. It seems possible that the resultant lymphangitis would result in scar formation sufficient in some instances to produce partial obstruction of the cystic duct, but only after repeated episodes made possible by many years of life. It is, of course, well known that in general, chronic cholecystitis is insidious and very slow in development (shown also in our experiments). This fact in itself is important in explaining the infrequency of chronic cholecystitis in childhood.

#### SUMMARY

Three different mechanisms of producing partial obstruction of the cystic duct have been devised: (1) Turning in a flap of gallbladder wall at the neck of the organ; (2) infolding of the wall at the neck by mattress sutures (tuck); and (3) crushing of the cystic duct. In every instance when a definite obstruction at the cystic duct was produced, a severe grade of chronic cholecystitis consisting of fibrosis, lymphocytic infiltration, *etc.*, similar or identical to that seen in human beings, was produced. However, the development is so slow that even minimum changes are not demonstrable until four to six months have elapsed since production of the lesion. Maximum effects are not noted until at least two years have elapsed since production of the obstruction. Gallstones were produced on two occasions.

No experiments were undertaken to demonstrate the mechanism of production of the cholecystitis, but it is assumed that the obstruction results in an overconcentration of bile salts and other chemical constituents of the bile, which, in turn, exert a damaging effect on the mucosa of the gallbladder through toxic chemical action. Infection appears to be a late event, and, presumably, is secondarily imposed upon the damaged gallbladder wall. In only 30 per cent of cases of experimentally produced cholecystitis was culture of the gallbladder wall and bile positive.

The first method mentioned, *i.e.*, turning in a flap of the neck of the gallbladder just above the opening of the cystic duct was by far the most effective technic in producing a partial obstruction—failing in only one instance. Controls consisting of infolding of a flap of gallbladder wall in the dome of the gallbladder, and ligation of the cystic artery, with accompanying lym-

phatics, did not result in pathologic changes in the wall beyond temporary edema (except at the immediate site of operation) in a single instance.

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DISCUSSION.—DR. DALLAS B. PHEMISTER (Chicago, Ill.): Doctor Cole has brought out the fact that there are many cases of gallbladder disease in which there is obstruction of the cystic duct, which are not due to a stone impacted in the duct. Now, the degree of obstruction in these cases is extremely variable. It may be slight, or it may be so extreme that no bile enters the gallbladder. In fact, every so often, we encounter a mucocele of the appendage, in which there is no stone either in the gallbladder or in the cystic duct.

An illustration shows a patient who had mild symptoms for about nine months, and cholecystography showed nonvisualization of the gallbladder. When the gallbladder was removed and cut open, thick mucus welled out. There were only a few flecks of pigment in it, and no sign of a stone. There was a chronic cholecystitis and also a chronic inflammation of the excised stump of cystic duct of somewhat comparable degree.

This cystic duct obstruction from noncalculus processes may cause a variation in the cholesterol, calcium and pigment contents of stones that form in the gallbladder, and, in general, the greater the degree of obstruction, the greater the likelihood that the stones will contain calcium and pigment; also, when the obstruction is of a high degree there may be free calcium in the gallbladder, as in the case illustrated by these lantern slides. The gallbladder was the seat of a mucocele, and, in addition, contained cholesterol-pigment stones and roentgenogram of an excised gallbladder in which there was no separate particles casting the heavy shadows of calcium carbonate. The cystic duct was the seat of a chronic obstructive cholangitis and free from stone.

Now, I have assumed the pathogenesis of these cases to be either a chronic cholecystitis, with extension of the infection to the cystic duct, or damage of the duct by passage through it of stones from the gallbladder. However, it is quite possible that Doctor Cole's explanation is correct, and that, in some cases, there are other factors that are responsible for duct obstruction.

DR. NATHAN A. WOMACK (St. Louis, Mo.): For a long time, the association between complete obstruction of the cystic duct and acute cholecystitis has been recognized. Doctor Cole and his colleagues have now shown definitely the relationship between partial cystic duct occlusion and chronic cholecystitis. One cannot easily find fault with either the experimental or clinical evidence that they have presented. The question that must be answered, however, is why does the obstruction produce the inflammation. Ordinarily obstruction produces distention. Obstruction produces inflammation only when the substance obstructed is injurious to tissue.

Recently, in a preliminary report, Bricker and I presented evidence to show that this injurious substance was bile. In the experimental animal, if the gallbladder is washed free of bile and filled with physiologic salt solution, complete obstruction of the cystic duct results in mucocoele. If the cystic duct is ligated without disturbing the bile in the gallbladder, a moderate degree of acute inflammatory change appears, which subsides. If, however, concentrated bile is placed in the gallbladder, severe inflammatory change is produced, and this seems to be almost in direct proportion to the concentration of the bile. Where half of the water is removed, gangrene of the gallbladder occurs in many instances. Various components of bile were studied, namely, cholesterol sodium deoxycholate, and sodium glycocholate and a solution of commercial dried bile, with comparable results. Inflammatory changes noted were identical to those seen in human cholecystitis, and were also similar to the cellular reaction seen when these substances are injected subcutaneously in the experimental animal.

We feel, therefore, that the etiology of cholecystitis is concerned with obstruction and imprisonment of bile, which becomes concentrated and, in turn, damages the gallbladder and perhaps liver tissue, leaving it susceptible to secondary bacterial invasion.

DR. W. H. COLE (Chicago, Ill., closing): I have merely one point to add, namely, to emphasize the fact that in these experiments we are dealing only with partial obstruction of the cystic duct. The relationship of complete obstruction of the cystic duct to gallbladder disease is well known. In three or four animals, we made a technical error and produced a complete obstruction of the cystic duct instead of a partial one; these animals were discarded.

## CEREBROSPINAL RHINORRHEA: SURGICAL REPAIR OF CRANIOSINUS FISTULA\*

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THE FAILURE of a craniosinus fistula with leakage of cerebrospinal fluid to close after the accepted procedure of suturing the rent in the dura, through a unilateral frontal craniotomy, prompted me to develop an operation which would effect permanent closure and cessation of the rhinorrhea.

This report includes a review of three cases in which the patients were successfully treated by the present method.† In the first case, cerebrospinal rhinorrhea occurred in a boy ten years of age, who had sustained a fracture of the skull involving both walls of the frontal sinus. Rhinorrhea had been present for eight and one-half years. In the second case, the patient was a man age 43, in whom rhinorrhea developed as the result of a fracture of the skull which extended into the cribriform plate of the ethmoid bone. The force producing the fracture came from a 50-lb. weight which was dropped on the vertex of the skull, producing a depressed fracture at the point of contact as well as a fracture involving the ethmoid. Although bloody discharge from his nose occurred at the time of injury, drainage of cerebrospinal fluid did not occur until six months later, at which time he appeared to have a head cold. Rhinorrhea continued for six months and endured until the time of his operation. In the third case, the patient was a woman, age 34, in whom spontaneous cerebrospinal rhinorrhea developed and was present for nine and one-half months. The cerebrospinal fistula in this case consisted of a communication between the meninges through the ethmoid into the nasal cavity. Craniotomy revealed an opening in the cribriform plate through which an olfactory nerve fiber descended; the opening was much larger than normal, being 2 Mm. in diameter. A villus of arachnoid extended through this opening into the ethmoid where, apparently, it had given away, accounting for the leak of cerebrospinal fluid. Normal relationships of the brain, meninges, and anterior portion of the skull are shown in Figure 1a.

*Causation.*—Cerebrospinal rhinorrhea may result from a number of causes, the most common of which is skull fracture that extends through the posterior wall of the frontal sinus (Fig. 1b) or the cribriform plate of the ethmoid bone, with accompanying tears of the dura and arachnoid.<sup>1, 7</sup> The first evidence of rhinorrhea associated with fracture of the skull is the occurrence of a watery, bloody discharge from the nose. In most instances, in my experience, the lesions heal with spontaneous remission of the rhinorrhea. Persistent rhinor-

\* Read by title before the meeting of the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

† Three additional cases have been operated with equally as good results.



rhea or the delayed occurrence of rhinorrhea usually is due to considerable loss of bone, absorption of a fragment of bone, or inclusion of the dura and arachnoid between fragments of bone which permits escape of cerebrospinal fluid into one of the nasal cavities. Cerebrospinal rhinorrhea frequently has occurred spontaneously, just as it occurred in my third case, and when it does occur, it probably is the result of a congenital defect in the cribriform plate which permits extension of an envelope of arachnoid along an olfactory nerve fiber through the cribriform plate. Leakage of cerebrospinal fluid undoubtedly is the result of rupture of the thinned-out arachnoid and mucous membrane. According to reviews in literature, precipitation of this type of rhinorrhea usually is the result of coughing or sneezing during an attack of head cold. Rhinorrhea has accompanied hydrocephalus, and in that particular instance leakage of cerebrospinal fluid was the result of increased intracranial pressure on thinned-out membranes and absorptive defects of the cribriform plate. I have also seen the condition afflict two patients suffering from pituitary tumor. The floor of the sella turcica had been absorbed, with presumable leakage of cerebrospinal fluid into the sphenoidal sinus. I also saw the condition in a patient who had a large osteoma of the orbit which had extended through the ethmoid into the anterior fossa. Rhinorrhea also has followed the removal of nasal polyps. The polyps probably were meningoceles that had extended through the cribriform plate. Rhinorrhea also has resulted from craniotomy when, in the making of the anterior margin of the bone flap, the frontal sinus was unintentionally opened.

*Symptoms and Signs.*—The only symptom that many patients complain of is an annoying, watery discharge of the nose. It may be continuous or cease for only a few hours before it continues. The discharge may appear as drops of clear fluid or it may pour out in a stream when the head is tilted in certain positions. Usually, it appears in one side of the nose and produces the sensation that is experienced when the nose is congested. In acute injuries of the head, it may be difficult to recognize cerebrospinal fluid because it is mixed with blood, but when the condition is chronic the fluid is watery and can be readily collected and examined chemically. Cerebrospinal fluid is colorless, limpid, slightly viscous, has a specific gravity of 1.004 to 1.008, and contains traces of protein and small quantities of inorganic salt and dextrose. The lymphocyte count varies from five to ten cells per cubic centimeter of fluid. If there is doubt about the presence of cerebrospinal fluid in a discharge from the nose, the indigo carmine test in which 1 cc. of indigo carmine is introduced into the subarachnoid space of the spinal canal by means of routine spinal puncture might be employed. Since the dye promptly stains the cerebrospinal fluid a bluish-green color will be seen to appear in the nasal discharge within about 15 minutes and will continue for two or three hours, if fluid discharging from the nose contains cerebrospinal fluid. This test is of particular value in the differentiation between cerebrospinal rhinorrhea and allergic and vascular rhinorrhea. Roentgenologic examination of the skull offers some aid in the diagnosis in cases of recent fracture, but rarely is such examination of much

assistance in the localization of cerebrospinal fistula involving the ethmoid cell.

Meningitis is the serious complication which may accompany this condition. It occurs more often when rhinorrhea results from fracture of the skull than it does when rhinorrhea occurs spontaneously, but it is a constant threat in all cases, and especially so when the patient has contracted a nasopharyngeal infection. Fortunately, chemotherapy has proved of value in combating meningitis and also has made it possible to perform these extensive operations without fear of the development of meningitis.

*Conservative Treatment.*—Conservative treatment (nonoperative) often has been employed by those who feared to advise or employ the radical procedure designed to close the fistulous tract. The argument set forth by those who advocate conservative treatment is that they believe it safer not to disturb the patient than it would be to hazard a radical operation. Unfortunately, there is little to offer in the way of nonoperative treatment. Fox,<sup>5</sup> and Friedberg and Galloway<sup>6</sup> reported two cases in which spontaneous cerebrospinal rhinorrhea was controlled by the application of a 20 per cent solution of silver nitrate. Fox identified the opening through the cribriform plate by the use of indigo carmine, after which he applied the solution of silver nitrate several times, with apparent recovery of the patient. Friedberg and Galloway stated that they observed the cerebrospinal fluid entering the nasal cavity at a point at which the anterior third portion of the middle turbinated bone joins the middle third portion of this turbinate, at which point they applied a 20 per cent solution of silver nitrate. The discharge ceased within 12 days and the patient had been free of rhinorrhea for 14 months, at the time of the report. Conservative treatment is of definite value in cases of acute rhinorrhea accompanying fracture of the skull, since a number of the meningeal defects will heal spontaneously. Teachenor,<sup>10</sup> Dandy,<sup>4</sup> Cairns,<sup>2</sup> Munro,<sup>8</sup> and Coleman<sup>3</sup> have advocated surgical repair of the meninges, if rhinorrhea does not disappear within four to six days after the time of injury. The approach employed is a transfrontal sinus approach, in which the dura is exposed at the point of injury. Teachenor has suggested removal of the posterior wall of the frontal sinus, along with craniotomy. Lesions involving the ethmoid and the overlying meninges have been dealt with more conservatively than this in cases in which the condition is acute. However, Coleman has employed unilateral frontal craniotomy in repair of recently injured meninges over the ethmoid bone. It has been my experience that if spontaneous recovery from cerebrospinal rhinorrhea is to take place after fracture of the skull, it may not do so for an interval extending from a few days to eight weeks, and, therefore, it has been my practice to limit the intake of fluid to 1,500 cc. per day, in order to decrease the output of cerebrospinal fluid, and to administer sulfanilamide or sulfathiazole in doses of 60 to 90 gr. (4 to 6 Gm.) per day, until the concentration of sulfanilamide in the blood registers from 8 to 12 mg. per 100 cc. Also, I have found it advantageous to have the patient remain in bed in a semi-erect posture, making sure that the patient sleeps in the same position, since this minimizes the flow of cerebrospinal fluid into the nose. In the event that

conservative measures fail to effect spontaneous remission of the rhinorrhea, I should advise the procedure employed in the treatment of the three patients to be mentioned herein.

*Surgical Treatment.*—Although fractures of the skull are common, a relatively small group develop cerebrospinal rhinorrhea. Coleman reviewed "940 cases of head trauma observed at the Neurosurgical Service, Hospital Division, Medical College of Virginia, in 1935-1936, there were 216 fractures of the skull, with 87 fractures of the base. Of the 87 basal fractures, 15 involved the frontal sinuses; six of these were associated with severe, compound, depressed fractures of the frontal vault, and operation was promptly performed for disinfection, débridement and closure of the dura." His observations are similar to those of others. The incidence of rhinorrhea after fracture of the skull varies from 2 to 5 per cent. In view of the fact that rhinorrhea sometimes is spontaneously cured, I am inclined to wait six or eight weeks before advocating repair of the craniosinus fistula unless the fracture is compound and involves both walls of the frontal sinus.

The accepted procedures for closure of craniosinus fistulae which communicate with the frontal sinus, ethmoid cells, and the nasal cavity have been: (1) In cases in which the condition is acute, surgical repair through the frontal sinus; (2) in cases in which the condition is chronic when it is possible to identify the site of the lesion, performance of small unilateral transfrontal craniotomy, identification of the fistula, and closure of the meningeal opening with interrupted silk sutures or closure of it with sutures and covering of it with muscle; and (3) performance of unilateral transfrontal craniotomy, in which the dura is elevated, the opening is identified and a wick of iodoform gauze is placed between the lacerated dura and the cribriform plate, as Peet has advocated. The end of the gauze wick is brought out through the frontal incision, but the wick itself is left in place for four days and then carefully removed. Peet<sup>9</sup> stated, "The object of this procedure is to prevent meningitis by allowing the brain to become firmly adherent to the lacerated dura thereby effectively closing off the subarachnoid space before organisms passing through from the nose can cause infection."

I have used these accepted procedures with varied success; the one difficulty that I always have encountered in attempting to free the dura from the cribriform plate is that the dura has had a tendency to tear, as Grant emphasized in his discussion of Coleman's paper. The dura, in addition to being thin, is likewise under moderate tension, which prevents the carrying out of proper overlapping of the dura which is necessary for thorough invagination of the meningeal fistulous tract. I have included muscle in the suture line to assure against leakage of cerebrospinal fluid. I have further attempted to assure against recurrence of rhinorrhea by filling the bony defect with Horsley's bone wax (Fig. 1c), but in spite of all these precautions, recurrence of rhinorrhea has occurred just as it did in the first case of this series. This failure prompted development of the operation employed in these cases of chronic rhinorrhea, in which cure has been obtained.

# CRANIOSINUS FISTULA

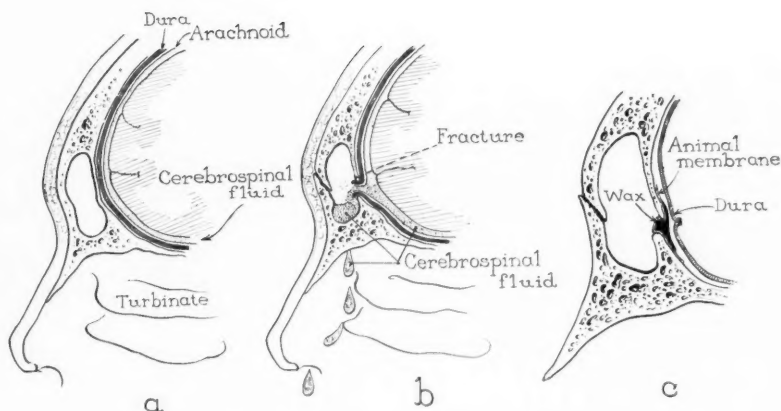


FIG. 1a.—Normal relationships of the brain, meninges and skull in the frontal region; *b*, craniosinus fistula with leakage of cerebrospinal fluid into the frontal sinus and thence into the nose; *c*, plastic closure of the meninges and occlusion of the bony defect with wax.

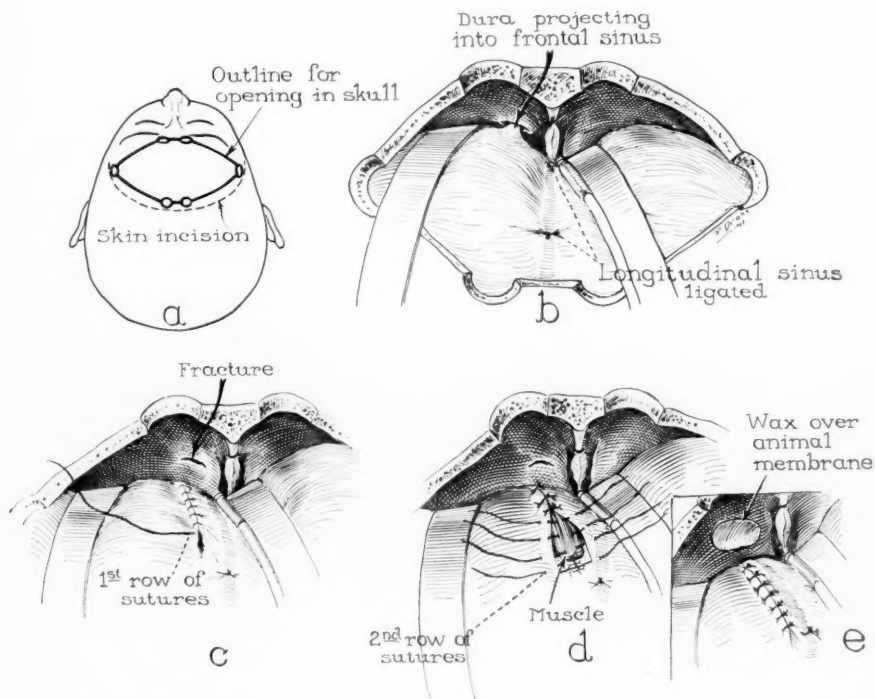


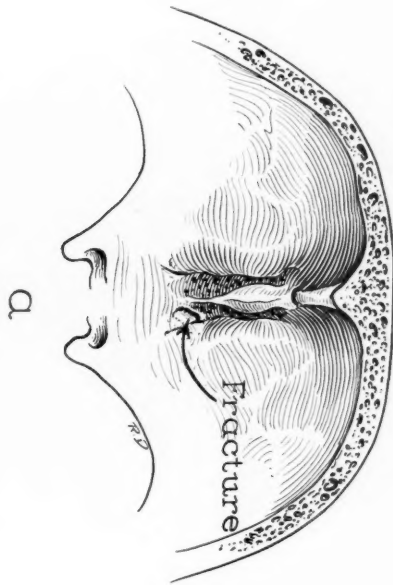
FIG. 2a.—Schematic outline of incision in the scalp and craniotomy; *b*, elevation of dura, identification of the fistulous tract and ligation of the longitudinal sinus; *c*, closure of the dural tear with a suture of continuous catgut; *d*, reinforcement of the primary closure by means of a second row of interrupted silk sutures, including a strip of muscle employed as additional protection against recurrence of the rhinorrhea; *e*, closure of bony opening with animal membrane and bone wax.

The procedure consists of performance of craniotomy which will allow the dura to be elevated from the bone in both halves of the frontal fossa. The bone flap must be designed so as to extend across the midline and to uncover the anterior poles of both frontal lobes (Fig. 2a). A coronal scalp-flap incision is employed. It is placed within the hairline, after which the scalp and periosteum are reflected forward to a line just above the frontal sinus. Six trephine openings are made, the first two of which are placed on each side of the midline just above the frontal sinus. The second two trephine openings are placed on each side of the midline and the longitudinal sinus, approximately 3 cm. in front of the coronal suture. The third two openings are placed in the temporo-frontal region, one on each side. As the bone between all the openings is cut with a Gigli saw, an opening is effected which is sufficient to permit elevation of the dura and the frontal lobes. The bone flap is kept sterile during the operation by means of a sponge soaked with saline solution. Caution is taken to avoid injury to the longitudinal sinus. Bleeding from the longitudinal sinus is controlled by ligation of the sinus (Fig. 2b) with silk ligatures at a level 6 cm. above the foramen cecum, which is situated superior to the crista galli. In some instances, it is necessary to ligate the longitudinal sinus where it communicates with the foramen cecum. The advantage of ligation of the longitudinal sinus allows the dura to be sutured into, and, if necessary, to be used in closure of the fistulous tract. The procedure is continued by elevation of the dura from the frontal fossa and the olfactory grooves, where it is necessary to sacrifice the olfactory nerves. The elevation of the dura is continued until the anterior crest of the sella turcica is approached. During this dissection, the fistulous tract is always encountered, whether it be situated on the right or the left side. The meninges will be seen to extend into the defect of the frontal sinus or the cribriform plate.

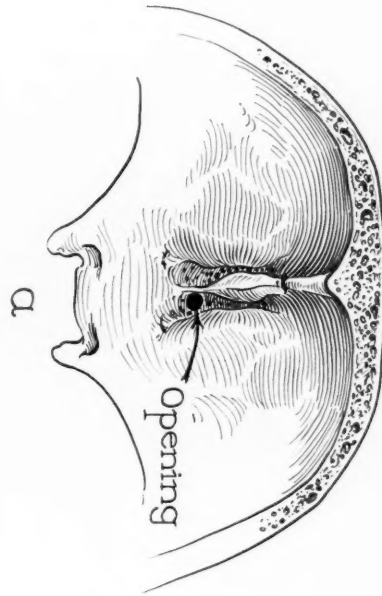
After the dura has been mobilized sufficiently and the fistulous tract identified, plastic closure of the tract is begun by overlapping of the dura in such a way as to invaginate the meningeal portion of the fistula. The first suture is placed in the most dependent part of the elevated dura (Fig. 2c). This suture is continuous chromic catgut No. 0. The primary line of suture is protected by a strip of muscle which is transfixed to the dura and further reënforced by the placing of a second row of interrupted silk sutures (Fig. 2d). The defect in the frontal sinus or cribriform plate is filled with Horsley's bone wax. Further to protect against forcing of the wax through the cranial defect into the sinus or nose, Lukens' animal membrane is placed over the defect before the introduction of wax to plug the hole (Fig. 2e).

The advantages of bifrontal craniotomy are: (1) A better exposure is obtained than by employment of a unifrontal flap; (2) the surgeon is always sure to identify the fistulous tract; (3) the exposure thus obtained affords a better opportunity for elevation of the meninges along the cribriform plate; and (4) after elevation of the dura from the cribriform plate, tension on the dura is relieved; this permits greater ease of invagination of the fistulous tract and successful performance of overlapping dural closure of meningeal defects.

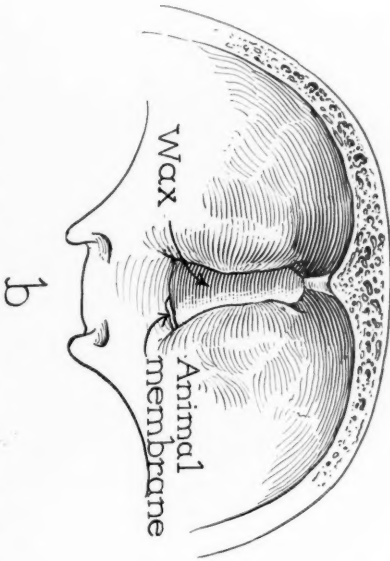




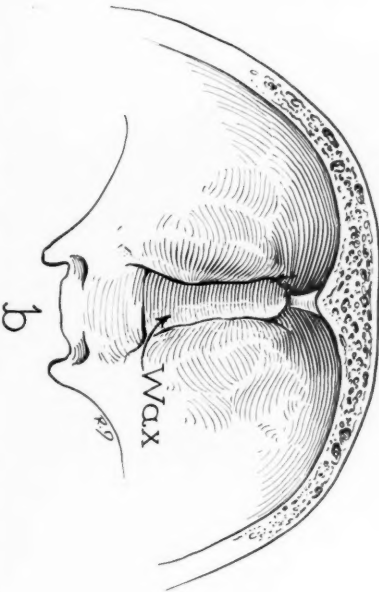
a



a



b



b

FIG. 3a.—Fracture of the cribriform plate; b, closure of the bony defect with animal membrane and bone wax.

FIG. 4a.—Congenital defect of the ethmoid bone, such as the third patient in this series had; b, closure of the bony defect with wax.

Before replacement of the bone flap, thorough hemostasis should be effected. A rubber tissue drain can be used, but is not necessary because no cerebrospinal fluid will be seen to escape. The bone flap is wired in place with noncorrosive wire, inserted through perforations which are placed opposite each other in the skull and bone flap. The periosteum, galea, and scalp are closed with interrupted silk sutures.

As a precautionary measure, administration of sulfanilamide is continued for three days prior to operation until the concentration of sulfanilamide in the blood reaches a value of from 8 to 12 mg. per 100 cc. Likewise, it is continued for ten days after operation, during which time the same concentration of the drug in the blood is maintained. The dosage I have employed, ranged from 45 gr. (3 Gm.) to 90 gr. (6 Gm.) per day. In no instance did meningitis develop during the postoperative period.

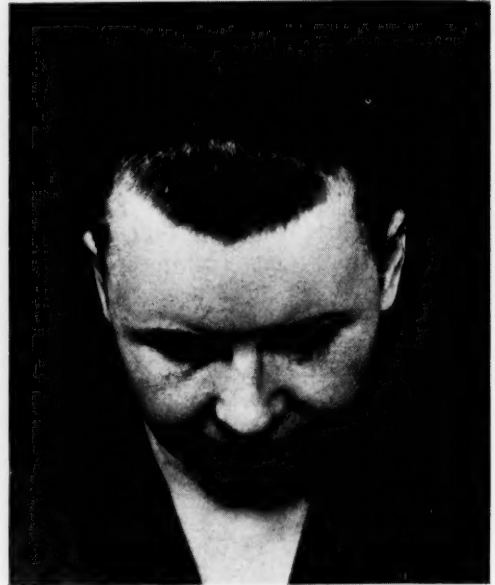


FIG. 5.—Postoperative appearance of the patient who had the congenital defect in the ethmoid bone shown in Figure 4a and b.

*Comment.—Three Cases of Craniosinus Fistulae:* Results of the method described for plastic closure of a craniosinus fistulous tract have been most satisfactory in all three cases mentioned herein, since all the patients underwent the operation without incident, all incisions healed by primary union, and cerebrospinal rhinorrhea ceased immediately after plastic closure. In the first case, meningitis afflicted the patient (a boy) ten months after operation, after an attack of influenza. This was controlled by chemotherapy with sulfathiazole, and at the present time he is in good health and has been free of rhinorrhea from the date of operation, 17 months ago. The second patient (Fig. 3a and b) is well and has returned to work as an engineer in an electric plant and has been free of rhinorrhea for seven months, at the time of writing. The third patient (Figs. 4a-b and 5) is well, has returned to normal activity, and has been free of rhinorrhea from the hour of operation, like the others, until the present time, a period of two months. The first patient had had two severe attacks of meningitis prior to his operation. In the second and third cases, in which there were lesions in the ethmoidal plate, the patients had escaped meningitis prior to operation. Postoperative sequelae did not develop in these two cases.

The operative procedure I have described may not be indicated for cerebrospinal rhinorrhea which accompanies acute compound fractures, but it does

offer an effective method for the control of rhinorrhea, especially so for those patients who complain of chronic rhinorrhea in traumatic cases of delayed and spontaneous rhinorrhea. The one objection to this procedure is the loss of the sense of smell which ensues, but if symptoms are to be relieved and the hazard of meningitis is to be minimized it becomes necessary for the patient to accept this particular sequela.

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## SURGERY OF HYPERPARATHYROIDISM: THE OCCURRENCE OF PARATHYROID IN THE ANTERIOR MEDIASTINUM AND THE DIVISION OF THE OPERATION INTO TWO STAGES\*

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THE TREATMENT of hyperparathyroidism is surgical. Irradiation therapy has so far proved unsuccessful,<sup>†</sup> and attempts to control the effects of the disease by diet have been injurious either to the kidneys or to the bones. The surgical treatment of hyperparathyroidism must be precise to meet the challenge of the diagnostician. Spingarn and Geist<sup>2</sup> have reported two cases in which the diagnosis is beyond question and yet in which no parathyroid tumor was found at operation. Nine patients have been referred to the Massachusetts General Hospital for further operation following unsuccessful explorations by other surgeons. In one of these, Case 50 of our series,<sup>‡</sup> the author was unable to find the adenoma at operation; its location was disclosed at autopsy. In the nine cases, the surgical problem has been one of the peculiar position of the tumor. All had large tumors and, from the point of view of size alone, none should have been difficult to find.

The problem of the surgery of hyperparathyroidism involves both site and size of the tumor. As more cases are recognized by the clinicians, size becomes increasingly important. Milder cases are being diagnosed and the milder the case, the smaller the tumor. Unless surgeons take cognizance of the peculiarities of parathyroid surgery, an increasing proportion of surgical failures may be expected. This paper is written to emphasize certain points already described,<sup>3, 4</sup> and to give in detail newer ideas in the operative management designed to obviate the difficulties which lead to unsuccessful explorations.

**REQUISITE TRAINING.**—The problems of parathyroid surgery are not those of the regional anatomy of the neck but are peculiar to the anatomy and physiology of the parathyroid glands. Special training is needed; the technical skill adequate for successful extirpation of the thyroid gland is not sufficient. The nine cases with previous unsuccessful attempts, mentioned above, were

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28–30, 1941.

† Four of the series of cases of hyperparathyroidism in this hospital received adequate roentgenotherapy before removal of the adenoma at operation; in none was there a demonstrable change in the abnormal metabolism. Reports in the literature of cases benefited by roentgenotherapy<sup>1</sup> do not include sufficient data of calcium and phosphorus metabolism for us to assume that the clinical improvement was not due to diet alone.

‡ The numbers refer to the cases of hyperparathyroidism at the Massachusetts General Hospital in the order in which the diagnosis is proven. The same case numbers are used in all publications from this hospital.

# HYPERPARATHYROIDISM

operated upon by 13 surgeons, all skilled in surgery of the thyroid gland. Not only were the tumors not found but several of the surgeons intentionally removed what they considered to be normal parathyroid glands, a procedure without justification.

*Recognition of Parathyroid Tissue.*—The eye must be trained to distinguish the varieties of parathyroid tissue. Beyond the variations in the glands of normal people there are differences in the uninvolved as well as the diseased glands of hyperparathyroidism. The training requires prolonged and precise observation and, apparently, cannot be obtained by operating upon the thyroid gland. There is but one place for this training and that the post-mortem table. Here, any debatable tissue must be immediately checked by frozen-section, since by the time permanent sections are ready the image of the gross appearance is forgotten and the chance for experience lost.

The size and shape of the normal gland show considerable variation (Fig. 1). The gland is soft, for it is composed of the parathyroid and fat cells, with but little supporting stroma. The capsule is thin, with a fine network of ves-

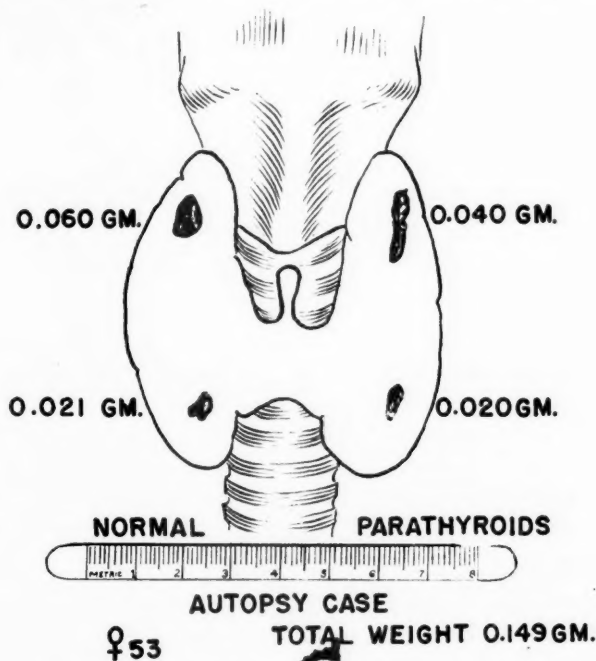


FIG. 1.—Four normal parathyroids, removed at autopsy, were photographed on a diagram. Variations in shape and size are shown (Churchill and Cope: *ANNALS OF SURGERY*, 104, 9, 1936.

sels over it. Because of the softness, the shape is determined by the surrounding organs which are firmer. The glands are flat like a pancake only if molded over the surface of an organ like the thyroid or esophagus. If they are free in fatty or areolar tissue they are globular, a form they also assume when within the thymus gland. They have a clearly formed vascular hilus with a fern-like pattern of vessels radiating out over the capsule.



The color of the gland varies, and depends upon the proportion of glandular to fat tissue. The fat content of the normal glands changes with age.<sup>5</sup> The gland of the child before puberty contains little or no fat and is, therefore, the coffee-brown color of the normal parathyroid cells. After puberty, until about age 40, the fat content increases and the glands, therefore, become yellower. After age 40, there may be a decrease in fat content with almost none in the older age-groups. With increasing experience in the identification of the uninvolved or so-called "normal" glands in patients with hyperparathyroidism due to adenoma, the author has been impressed with the abnormal yellowness. It is believed, though not proven histologically, that, in the presence of an active tumor, there is an atrophy of disuse of gland cells, with a relative increase in the fat cells. Since the uninvolved glands may be so nearly the color of the surrounding fat the only means of distinguishing them is their encapsulated form and vascular pattern.

Both the adenomata and hyperplastic glands contain little or no fat and are, therefore, browner than any normal tissue. Although we have only had experience with six cases, it is believed that the hyperplastic glands are somewhat different from the adenomata; the color is a shade deeper; the surface is uneven instead of smooth; and the gross contours are more irregular.

*Meticulous Technic.*—The importance of a careful, bloodless technic has been stressed in previous publications.<sup>3, 4</sup> Even the slightest trauma to a parathyroid gland may result in the spread of a subcapsular hematoma, changing the appearance to that of thyroid or an hemolymph gland. Inadequate hemostasis may result in diffusion of blood through the areolar tissue, beclouding the presence of a normal gland or small adenoma. In an operation for hyperparathyroidism there is no place for haste.

*Understanding of Parathyroid Physiology.*—The surgeon should be conversant with the abnormal physiology of the parathyroid glands. The search at operation for parathyroid tissue may be prolonged. The conviction that the patient has hyperparathyroidism may serve to drive the surgeon forward to the goal.

Once the offending gland or glands are isolated, the surgeon must exercise judgment in what to do with them. Not only must he avoid producing hypoparathyroidism but also appreciate the relation of the renal and bone complications of the disease to the tetany of the recalcification period.<sup>4</sup>

*WIDESPREAD DISTRIBUTION OF PARATHYROIDS.*—It is not enough to know what parathyroid glands look like; knowledge of the regions in which they are to be found is equally important. Perhaps the name parathyroid is unfortunate for it suggests that these glands exist only in a limited area near the thyroid. Indeed, this concept has arisen; the initial clinical interest in these glands was occasioned by the desire to avoid them in performing a thyroidec-tomy, and anatomic studies of their distribution were made by men primarily interested in the problems of thyroid surgery. The widespread distribution of parathyroid glands which may occur normally has been a product of embryologic study. This problem of distribution has become clarified in our

## HYPERPARATHYROIDISM

minds owing to the number of our cases in which a mediastinal parathyroid tumor has been discovered.

*Incidence of Parathyroids in the Mediastinum.*—At the Massachusetts General Hospital there have been 60 cases of hyperparathyroidism. The diagnosis was proven in 58 at operation, in two, at autopsy. In 54, the disease was due to adenoma, in six to primary hyperplasia. Of the 54 cases due to adenoma, four had two adenomata, the rest only one.\* This makes a total of

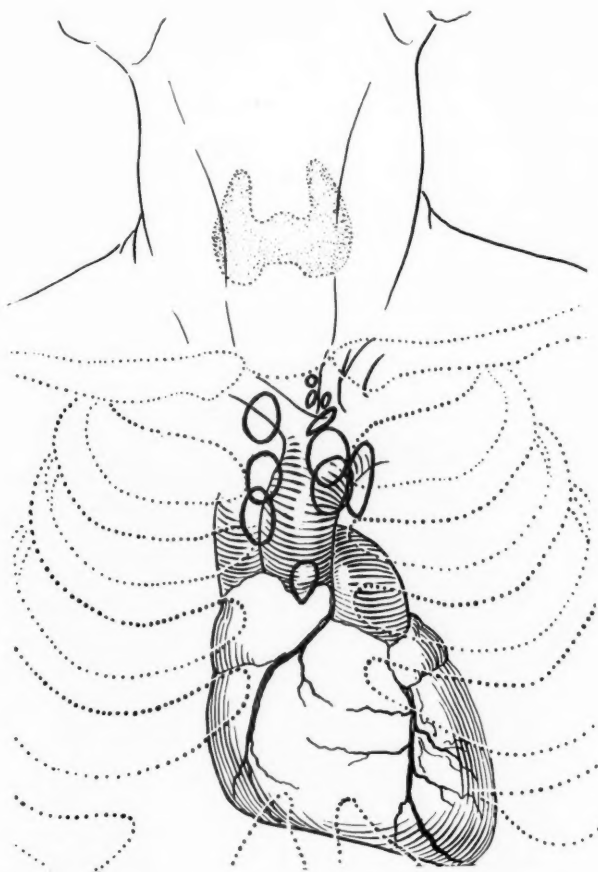


FIG. 2.—Diagram of position and size of the parathyroid adenomata recovered from the anterior mediastinum in 11 patients of this series.

58 adenomata; 11 were found in the anterior mediastinum (Fig. 2), and 5 in the posterior, the remainder in the neck. Of the six cases of primary hyperplasia, 23 individual glands were identified at operation; all lay in the neck, except one which was in the posterior superior mediastinum. The twenty-

\* Two of the cases with one adenoma already removed show some degree of residual disease and are believed to have another adenoma, in the mediastinum. The second-stage operation has been postponed.

fourth gland, which was not disclosed (Case 15), presumably lay in the anterior mediastinum.\*

Of the nine cases previously operated upon by other surgeons and referred to this hospital for further operation, in six, the adenoma was found in the anterior mediastinum, in one, in the posterior; in only two, were the adenomata in the neck. The position of the adenoma within the chest in seven of the cases presumably accounted for the failure of the search. From a statistical point of view, the nine cases constitute a selected group, and should be eliminated from consideration of the probable incidence of parathyroids within the mediastinum. With these nine cases excluded, nine of 49 adenomata (18 per cent) were in the mediastinum; five (10 per cent) were in the anterior mediastinum; four (8 per cent) in the posterior.

*Reasons for Mediastinal Position.*—There are two causes for the presence of parathyroid enlargements within the mediastinum:

(1) EMBRYOLOGIC DESCENT.—In the series of patients with hyperparathyroidism at this hospital, parathyroid glands have been encountered from 1 cm. above the upper pole of the thyroid gland down into the mediastinum as far as the pericardium. These extremes in distribution are accounted for by the embryologic development of the parathyroid glands. Excellent accounts of the embryology of the parathyroid glands and their associations with the development of the thyroid and thymus glands are given in the monographs by Weller,<sup>6</sup> and Norris.<sup>7</sup>

The parathyroid glands develop as two pairs from two separate bilateral primordiums in conjunction with the thyroid and thymus glands. The development of the so-called upper pair of parathyroid glands is the simplest. They have their origin in a primordium arising from the fourth branchial cleft. The parathyroid cells appear above and behind the lateral thyroid component arising from the same cleft and descend in this relation to the lateral thyroid as it grows down in the neck to join the median thyroid component. Since the lateral thyroid component travels only a short distance during embryonic life, from just below the upper portion of the larynx to the normal thyroid position opposite the cricoid cartilage, the parathyroid IV (upper parathyroid of adult life) also travels a short distance only. The upper parathyroid of the postfetal human being, from the embryologic point of view should, therefore, exist only in an area bounded above by the upper border of the larynx and below by the lower pole of the thyroid. Theoretically, they should not occur as low as the lower pole of the thyroid.

In actual observation of patients at operation, in which it has been possible to identify definitely the upper from the lower parathyroid, only once has a normal upper gland been disclosed below the main branch of the inferior thyroid artery. It is often encountered in the upper branches of the inferior thyroid vessels but more often lies nearer the upper pole. Embryologically, it should be situated posterior to the thyroid but actually this is not always

\* This patient died at home, presumably of cardiac failure; no postmortem examination was obtained.

## HYPERPARATHYROIDISM

the case. In two patients, the upper glands have been isolated anterior to the superior thyroid vessels; one adenoma and an occasional normal gland have been revealed between the upper pole and the larynx. Largely because of the limited area of embryologic descent, the upper parathyroids have been much easier to identify surgically (Fig. 3).

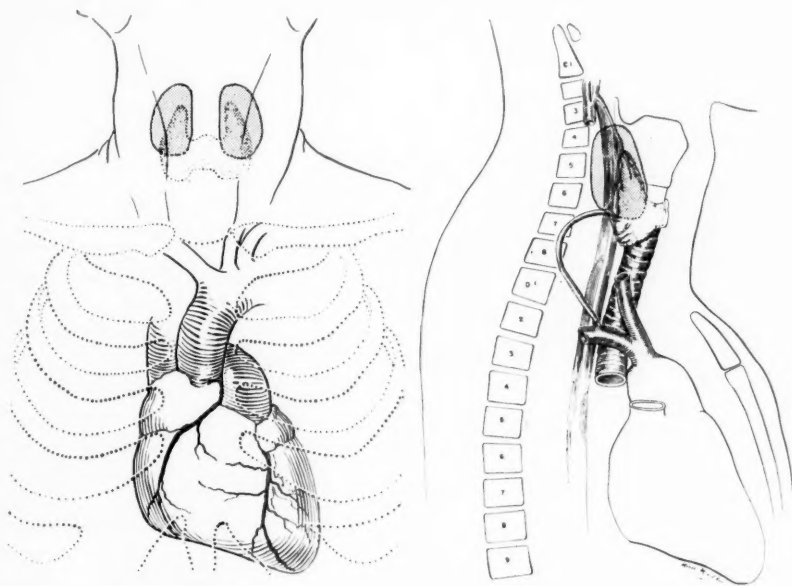


FIG. 3.—Lateral and anterior views of area of occurrence of upper parathyroid (IV) due to embryology. The shading shows the extent of possible positions of the upper parathyroids due to differences in development during fetal life. The limited area facilitates the surgical identification of these parathyroids.

Not so the lower parathyroids. In their embryologic development they cover a wide field and their discovery in postfetal life presents the major surgical difficulty of hyperparathyroidism. The lower parathyroid develops on either side from the third branchial cleft in close proximity to the primordium of the thymus gland. As the thymus tissue grows and moves downward in the neck from the pharynx to its final position in the anterior mediastinum, the parathyroid tissue descends with it. Such is the proximity of this parathyroid to the thymus that Weller<sup>6</sup> has well called it the "parathymus" gland. In the majority of cases examined by embryologists, these parathymus glands pass with the thymus lateral to the upper parathyroid and lateral thyroid component and are dropped off opposite the lower pole of the thyroid. The thymus continues its growth into the thorax. Sometimes, however, the parathymus gland grows with the thymus on beyond the lower pole of the thyroid and deposits itself either low in the anterior neck or in the chest. The association may end with the parathyroid still within the capsule of the thymus.

Reports have appeared<sup>8</sup> of intrathymic normal parathyroids in the human being. We have seen no reports of parathyroid tumors within the thymus.

The intrathoracic tumors reported in the previous communications from this hospital<sup>3, 4</sup> were free in the areolar tissues of the mediastinum and not within the thymus. Of the five subsequent tumors excised from the anterior mediastinum, three were within a well-defined thymic capsule. The intrathymic existence of the parathyroid gland is more common, we believe, than previously suspected. It is important to stress that parathyroids are to be found not only in the upper portion of the thymus as one would expect on embryologic grounds but also in the lower portion as well (Case 50, Fig. 11).

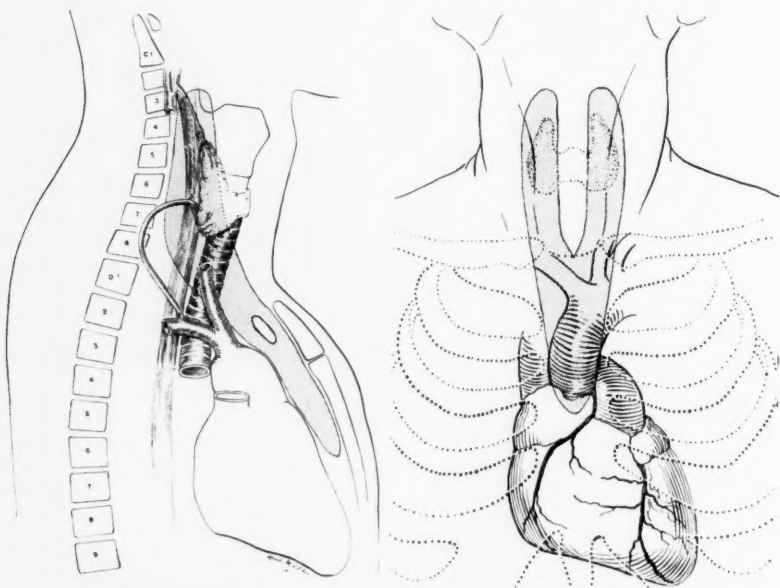


FIG. 4.—Lateral and anterior views of area of occurrence of lower parathyroid (III) due to embryology. The shading shows the extent of possible positions of the lower parathyroids due to differences in development during fetal life. The extensive area accounts for the surgical difficulty frequently encountered in identifying these glands. The glands lie anterior or posterior to the left innominate vein.

The parathyroid gland in this patient was in the lowest position of any gland we have observed. A gland outside of the thymus might, theoretically, be in a similarly low position. It is possible, though doubtful, that parathyroid tissue might descend lower than the thymus; since the position of the thymus in the anterior mediastinum is variable, the lowest point at which parathyroid tissue might be encountered is also variable. The area in which the lower parathyroid gland is to be expected on an embryologic basis is shown in Figure 4. The uppermost level is theoretically higher than that of the upper parathyroid. No upper gland has been observed in our series above the upper pole of the thyroid.

The relations anteriorly and posteriorly are shown in the illustrations. In its descent, the thymus tissue passes anteriorly to the great arteries but not necessarily to the innominate veins. At three operations, at which the thymus could be definitely identified, it encircled the left innominate vein but lay in



front of the aorta, the innominate, and carotid arteries. The parathyroids in the anterior portion of the superior mediastinum have borne this same relation to the great vessels. In the anterior mediastinum proper, only those glands that were within the thymus have actually lain in front of the aorta. Those lateral to the thymus have dropped posteriorly into the middle mediastinum, lateral to the aorta.

Reports have appeared<sup>9, 10</sup> emphasizing the occurrence of parathyroid tumors within the substance of the thyroid gland. Embryologically, the upper parathyroid could, theoretically, be included within the thyroid, much as the lower parathyroid is caught in the thymus. Such a position within the thyroid is less likely to be assumed by the lower parathyroid; it might, however, get caught in the sulcus of the expanding thyroid. Indeed, we have not infrequently found both upper and lower parathyroids deep in sulcuses of the thyroid, even completely buried from view, but we have not observed a true intrathyroid parathyroid, normal or tumor.

(2) DISPLACEMENT FROM NECK INTO MEDIASTINUM.—It is believed that enlarged parathyroid glands may be displaced from their position of embryologic development in the neck into either the posterior or anterior portions of the superior mediastinum. No gland has been followed through such a trek but the assumption is made on the basis of indirect observations: First, enlarged parathyroid glands have been found in the posterior mediastinum where, embryologically, no parathyroid tissue should exist. Second, all of the enlarged parathyroids encountered in the posterior mediastinum have had long vascular pedicles leading up to one or other group of thyroid vessels. In contrast, the blood supply of enlarged parathyroids in the anterior mediastinum occurs locally with no connection to the thyroid vessels. For example, in Case 57 the arterial supply arose from the middle mediastinum along the pleura, with the main venous return emptying into the left innominate vein; in Case 54 the artery came from the pericardial vessels, with the largest vein again leading up into the innominate.

Third, no normal gland has been found straying far from its vascular base. The normal gland is supplied by a fine twig from the nearest artery; if the gland lies near the upper pole of the thyroid, the twig comes from the superior thyroid artery or one of its branches; if near the lower pole it originates in a branch of the inferior thyroid artery; if between upper and lower poles, the parathyroid artery may come from the anastomotic branch between superior and inferior thyroid arteries. It is, therefore, believed that the normal parathyroid receives its blood supply from the region in which the gland was finally deposited during embryologic development and that the origin of the arterial supply should give the clue to this region if the gland were displaced.

Fourth, the parathyroid gland is held in position largely by its vascular pedicle. The capsule has only filmy connections with the surrounding tissues and unless caught in a sulcus, for example in the thyroid, the gland is movable. This is in contrast to the thyroid gland which has firm fascial attachments to the cricoid cartilage and upper trachea which cause it to move with larynx

and trachea on swallowing. When a parathyroid gland enlarges, it can be readily displaced by the surrounding organs. The vascular pedicle should offer but little resistance to downward displacement. Thyroid enlargements when freed of fascial attachments by continued growth are readily drawn into the mediastinum in spite of their vascular connections.

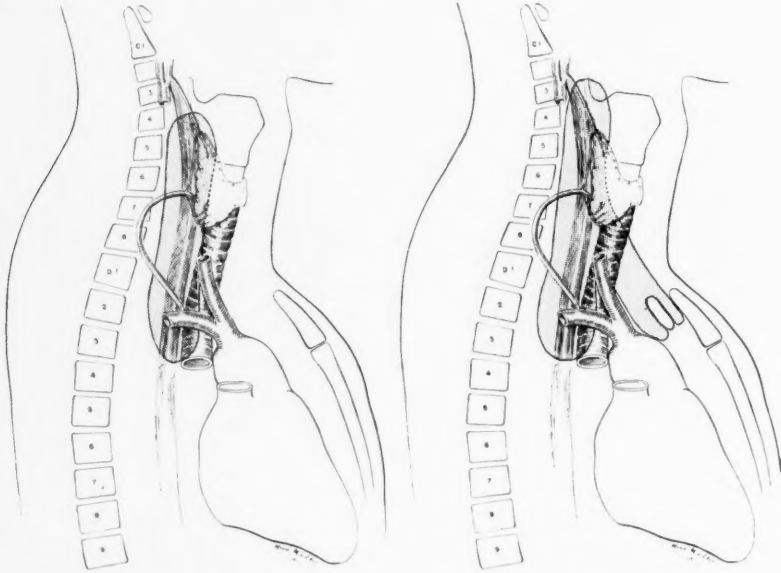


FIG. 5.

FIG. 6.

FIG. 5.—Lateral view of area of occurrence of enlarged upper parathyroid (IV). The original area of embryologic occurrence (Fig. 3) is added to owing to displacement downwards of enlarged glands. Because the only embryologic position permitting displacement is the posterior one, enlarged glands move toward the posterior superior mediastinum.

FIG. 6.—Lateral view of area in which enlarged lower parathyroids (III), displaced from their original position in neck, may be found. Glands having had embryologic position posterior to thyroid, after enlargement may be displaced into posterior mediastinum; those having had embryologic position caudal to thyroid in a more anterior plane, may be displaced into the anterior superior mediastinum.

Fifth, three times an enlarged upper parathyroid has been disclosed straddling the inferior thyroid artery like a saddle on a horse's back; it is believed that the gland was caught by the artery on its journey.

The passage of an enlarged parathyroid downward is presumably initiated by the weight of the gland itself but is accelerated as it approaches the thorax by the negative intrathoracic pressure. Depending upon the original position of the gland, the enlarged gland may be sucked into either the posterior or anterior mediastinum. If the gland was originally an upper one, it passes downward into the posterior mediastinum if it is not caught on the inferior thyroid artery (Fig. 5). If the gland was originally an inferior parathyroid lying posterior to the lower pole, it also will be sucked into the posterior mediastinum. If, however, it lay caudal to the thyroid lobe, in which case it will be in a more anterior plane, it may be drawn into the anterior superior mediastinum (Fig. 6).

Walton<sup>11</sup> was the first to describe the probable descent of enlarged parathyroids from neck into mediastinum. He conceived of various fascial planes which decided whether the enlarged gland descended into the posterior or anterior position. We have been unable to confirm the existence of these fascial planes and believe that the direction taken is due rather to the original position of the gland as a result of its embryologic development. Once these glands have reached the mediastinum they presumably do not go any further since the negative intrathoracic pressure no longer exerts a pull upon them.

The distribution of parathyroid glands may be summarized as follows: The upper glands (IV), when normal, exist in a limited area near the upper thyroid gland; when enlarged they may be displaced toward the posterior mediastinum; surgically they are easy to find. The lower glands (III), sometimes called the parathymus glands, when normal, are to be found over a wide area, from larynx to anterior pericardium; when enlarged this area may be increased to include the posterior superior mediastinum; their identification may require extended search. Enlarged parathyroid glands may exist in the mediastinum in more than 10 per cent of cases of hyperparathyroidism, and the surgeon must be prepared to meet this eventuality. Although a vascular pedicle leading to the mediastinum should be sought when exploring the thyroid region, its absence does not exclude a parathyroid in the anterior mediastinum.

**OPERATIVE TECHNIC.**—The not infrequent presence of parathyroid glands within the mediastinum has necessitated a reconsideration of the operative plan. Although early in our experience we met with some success in delivering enlarged parathyroids from the mediastinum by blunt dissection with the fingers, later failures emphasized the importance of direct visualization of tissues. The neck is first explored as heretofore, and if all of the offending glands are not disclosed the anterior mediastinum is opened through the sternum at a second operation.

*First Stage.—Exploration of Neck and Posterior Mediastinum:* The regions of the neck and posterior superior mediastinum in which parathyroids may be found, can be explored adequately under direct vision through a wide collar incision in the lower neck. The platysma is elevated with the skin flaps. The sternomastoid muscle is dissected free of the sternohyoid and omohyoid muscles opposite the cricoid cartilage but only enough to expose the ansahypoglossal nerve. The sternohyoid muscles are divided in the midline from the thyroid cartilage to the manubrium. Stitch ligatures are placed around the larger veins lying in the fascia on the anterior surface of the sternohyoid muscle. The muscle is cut from medial to lateral. The small artery lying near the medial border is ligated. The sternothyroid muscle is thus exposed and it is divided at its insertion to the larynx. The ansahypoglossal nerve is spared as it passes along the posterolateral border of this muscle to supply the lower portions of both the pretracheal muscles. Retraction sutures are placed through the upper end of the outer muscle only and the lower ends of both muscles, retracting them from the thyroid gland.

Large clamps are no longer used in dividing the pretracheal muscles, since to some extent their insertion is blind and the fine vessels leading directly from the surface of the thyroid into the sternothyroid muscle may be torn, with resulting hemorrhage. Wider exposure is obtained by retracting the entire sternothyroid muscle downward. Healing is better since the amount of necrosed muscle is decreased.

Before division of the pretracheal muscles, the contours of the thyroid prominence are carefully inspected. If there is any apparent difference, the larger side is exposed first. Such a difference due to a parathyroid tumor is rarely seen; it is more often due to asymmetry of the thyroid. In the absence of a demonstrable tumor mass directing attention to a special area, one lateral thyroid lobe is exposed. Traction sutures of silk rather than hooks are placed in the thyroid. In exposing the thyroid, pains should be taken to get in the fascial plane as near the true thyroid capsule as possible. If too much areolar tissue is left over the surface of the thyroid, parathyroid tissue may be retracted with the thyroid and difficulty encountered in exposing the thyroid sulci.

The search now proceeds on the basis of likelihood. Since the upper parathyroids occur in a smaller area it is sound policy to look for this gland first; it should be sought in the region from the inferior thyroid artery up to and above the upper pole. The gland may lie on the lateral, posterior, or medial surface.\* Both the superior and inferior laryngeal nerves may be exposed. If the upper gland is not revealed on the initial search, the region of the lower pole is next explored. If an apparently normal upper parathyroid was isolated, it is wise to proceed to the opposite side of the neck and look for the corresponding upper gland before exploring for the lower gland of the same side. This shift of side is made because of the probability that the glands are arranged symmetrically (see page 722), *Symmetry of Position*), and it may thus be possible to uncover rapidly 50 per cent of the glands.

When the regions of the lateral thyroid lobes have been thoroughly searched without finding the offending gland or glands, the dissection is then widened. The area above the upper pole as high as the upper border of the larynx is opened and the areolar tissue as far lateral as the carotid sheath is explored. The carotid sheath itself should be inspected.† The esophagus should be examined because a gland may hide behind it or between it and the trachea. The absence of a vascular pedicle along the esophagus is usually sufficient evidence to exclude a gland. In this plane, the sympathetic nerve trunks are uncovered. Next, the dissection is carried down into the posterior superior mediastinum on

\* Parathyroid glands have been reported on the anterior surface of the thyroid gland.<sup>12</sup> We have never encountered them in this position. It may be that a parathyroid gland on the lateral surface of the thyroid may assume an anterior position as a goiter develops.

† Norris<sup>7</sup> believes it possible on embryologic grounds for parathyroid tissue to become included within the carotid sheath. Although the sheath has frequently been opened in the cases operated upon at this hospital, no parathyroids have been encountered in this position.

either side, a feat easily accomplished since the line of vision is direct. On the left side, it is wise to identify the thoracic duct in order to avoid injuring it. Finally, the anterior superior mediastinum is sifted but only as far as direct visualization and dissection with instruments is possible.

**CONSIDERATIONS PECULIAR TO FIRST STAGE.**—*Vascular Pedicles:* The use of the identification of vascular pedicles leading into the superior mediastinum has already been pointed out. Such a pedicle leading in an atypical manner from one of the thyroid arteries may give an immediate clue to the position of a diseased parathyroid. In Case 53 the right upper parathyroid, an uninvolvement gland, had been identified; the left upper was not present in the symmetrical position. A small arterial twig, however, was seen leading up from the anastomotic artery to the space between thyroid and larynx where no artery normally runs. Dissection of the posterior thyroid region revealed no parathyroid tissue. Pursuing the vascular pedicle, the thyroid was separated from the larynx and upper trachea anteriorly and a small, flattened adenoma promptly found.

*Thymic Rests:* Rests of thymus tissue may also be a clue pointing to parathyroid tissue. These rests are not uncommon in the neck as well as mediastinum, and are due to remnants of tissue dropped off as the thymus descends from primordium to mediastinum. Since these rests are presumably pieces of the uppermost portion of the developing thymus, that portion with which the parathyroids III are closely associated, parathyroid tissue may adjoin if not lie within their capsule. Thymus rests should never be resected until it is certain that no parathyroid tissue is enclosed within them.

In addition to isolated remnants, there may be a well-defined tongue of the thymus gland rising toward the lower pole of the thyroid from the anterior mediastinum. In Case 47 after the identification of three normal glands, the adenoma was found within the capsule of such a tongue. In another patient, a normal gland lay within a tongue of thymus. In a patient recently operated upon for hyperthyroidism, rests of thymus tissue were encountered on either side behind the upper poles of the thyroid. Normal parathyroid glands were identified, one outside the thymic capsule and one within.

*Subtotal Resection of the Thyroid:* If the capsule and sulci of the thyroid gland have been carefully explored, actual resection of the thyroid gland should rarely be necessary. As mentioned above, under Embryologic Descent (page 710), parathyroid tissue, theoretically, may occur within the true capsule of the thyroid gland; none has been seen in this position in this hospital. Normal and enlarged glands have been found deeply buried in sulci but they have been outside the true capsule of the thyroid. It is possible that some of the "intrathyroid" parathyroids reported in the literature may have been placed in a position similar to ours.

*Second Stage.*—*Exploration of Anterior Mediastinum:* The anterior mediastinum cannot be explored under direct vision through an incision in the neck. The plane of the anterior space beneath the sternum lies at a right angle to the surgeon's line of vision. The only way to see into the anterior mediasti-



num is to open into it through the sternum. Adequate exposure of the anterior space is obtainable through division of the midline of the sternum from the notch of the manubrium to the level of the third interspace.

The skin is incised from the neck scar to below the third interspace and the midline of the sternum exposed. The pretracheal fascia is divided in the midline just above the manubrial notch and separated from the posterior periosteum of the manubrium. A finger is then inserted posterior to the manubrium

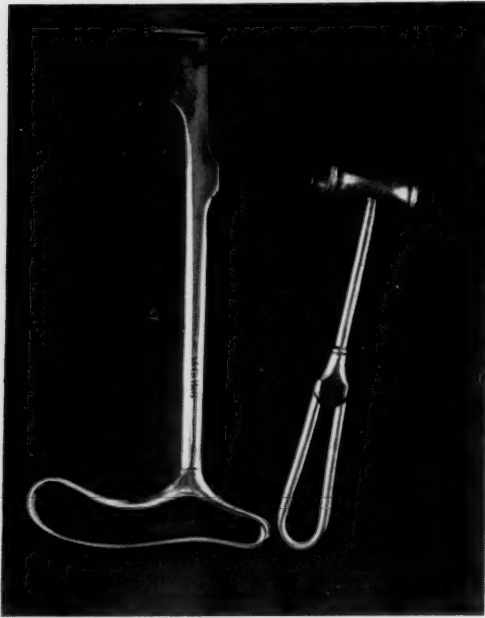


FIG. 7.—Lebsche sternal knife with mallet used for cutting the sternum.

and worked downward behind the sternum, pushing the pleura laterally and creating a space for cutting the sternum. On one side an opening, medial to the internal mammary vessels, is made into the cavity behind the sternum from the third interspace, and again, by blunt dissection, the pleura reflected laterally. The tunnel starting at the manubrium is now connected with the third interspace. The sternum is cut with a Lebsche sternal knife (Fig. 7), an instrument preferable to the Gigli saw, bone cutters, or rongeurs. The sternum is divided into two or three portions, depending upon the exposure needed. By incising from manubrium to the third interspace on one side, a good view of that side

of the anterior mediastinum can be obtained (Figs. 8 and 9). If the parathyroid gland is not found on that side, the third interspace of the opposite side is exposed and the sternum divided into it also. By this cut, the sternum is divided into three pieces and a wider exposure of the mediastinum obtained (Fig. 10). The longitudinal halves of manubrium and upper body of the sternum form two of the pieces and are retracted laterally. The lower undivided body is the third part and can be pulled downward and outward to expose the anterior pericardium. This third part with its attached costal cartilages forms the keystone of the anterior arch of the chest. Splitting of the sternum further down the midline diminishes the stability of this arch and the added exposure is not required.

The angle of the cut in the sternum from midline to third interspace is best made at 45 degrees. If both interspaces have to be opened into, the inverted V formed will aid the immobilization of the sternal fragments on closure.

After dividing the sternum, strict hemostasis must be secured by use of bone wax and silk sutures before any dissection is carried out within the

FIG. 8.—Initial cut of sternum partially made using sternal knife. Incision was started in right third interspace running towards notch of manubrium (Case 55, re-touched photograph of operation). Insert is diagram of incisions of sternum.

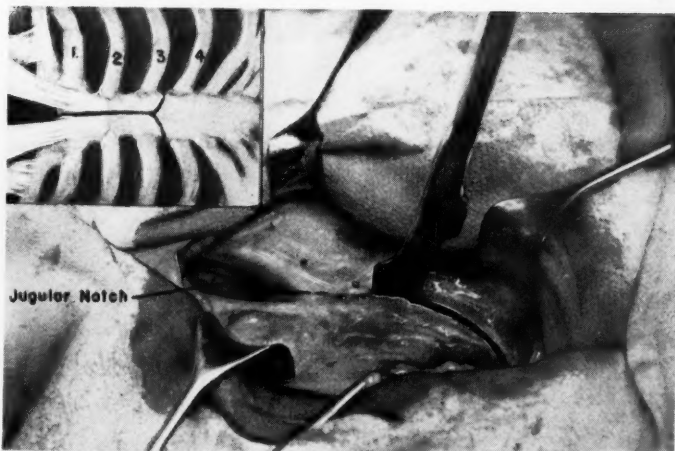


FIG. 9.—Anterior mediastinum exposed by retracting sternum after initial cut. View limited to the right side (Case 55).

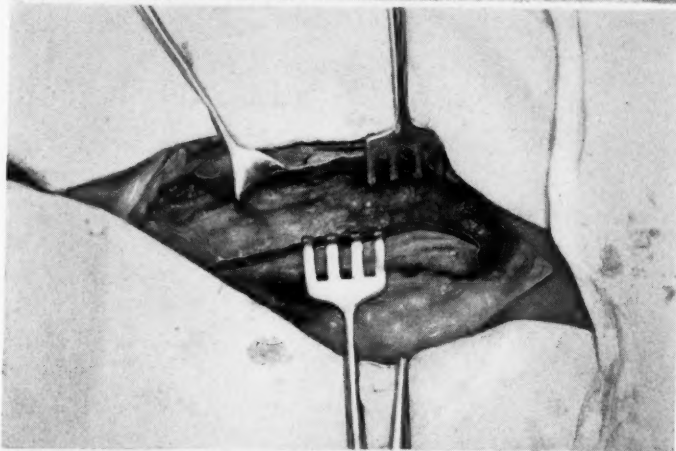
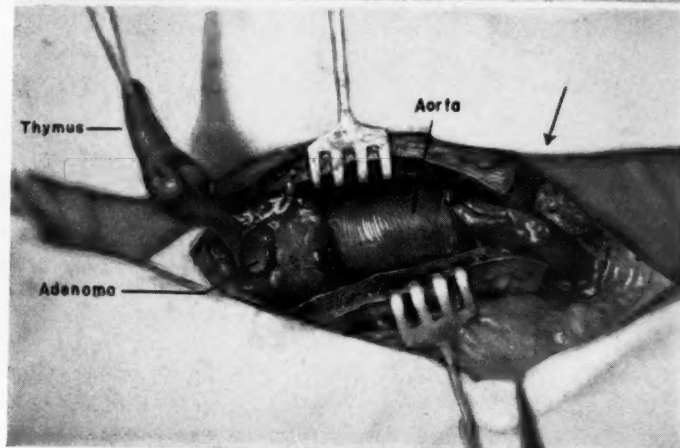


FIG. 10.—Exposure of anterior mediastinum increased by second cut of sternum into left third interspace; Arrow points to cut. The thymus gland is retracted out of the operative field. The parathyroid adenoma, dissected out of the thymus capsule, lies at the base of thymus on a pad of mediastinal fat. The aorta is shown between the retractors, caudal to the fat pad (Case 55).



thorax. The same particular technic used in the exploration of the neck must be employed, otherwise a small adenoma will be overlooked.

In the first dissection, the pleura on both sides is identified and displaced laterally. The great vessels are then uncovered; the remnant of the thymus should be encountered.

As far as we know now, the extent of the search within the mediastinum should be from the neck down to the right auricle and upper reflections of pericardium. The tumors are not found merely in the actual anterior space but may be displaced posteriorly on either side of the aorta, lying actually in the middle mediastinum against pleura and lung root. The tumors have been both anterior and posterior to the innominate vein. Apparently this vein lies in the middle of the path of embryologic descent of both thymus and parathyroids, whereas the arteries lie posterior.

In order to prevent as much postoperative discomfort as possible the sternum should be sutured firmly. The best closure has recently been obtained with stainless steel wire, which has sufficient tensile strength to be drawn tight and yet can be manipulated with ease.

On closing, all air and fluid should be removed from the mediastinum by suction and the absence of pneumothorax confirmed clinically, or roentgenologically if there is any doubt. Closure is made without drainage.

The anesthetic of choice for both operations is intratracheal gas-oxygen-ether. In the second, provision for positive pressure is made.

**CONSIDERATIONS PECULIAR TO SECOND STAGE.**—*Exploration Defined by Thymus:* Much time may be saved by exposing the thymus gland. In the first place, parathyroid tissue will probably not occur lower in the chest than the thymus and once the lowest point of the latter has been determined, at least the first dissection should be done from there upward. In the second place, normal parathyroids and parathyroid adenomata may be found within the thymus capsule; the adenoma in three of our cases has been so situated. One of these was not discovered until the portion of thymus lying behind the left innominate vein was freed. In the third place, since the parathyroids descend in intimate relation to the thymus gland in embryologic life, if a parathyroid is not within the thymic gland substance it may be expected to be close by.

In exposing the thymus, care must be taken not to resect it or jeopardize its blood supply unless it is certain that it contains no normal parathyroid tissue. The warning against resecting normal parathyroids applies, therefore, to resecting the thymus (see page 722), *Uses of Exposed Uninvolved Glands*).

**CONSIDERATIONS APPLICABLE TO BOTH STAGES.**—During either operation the following observations should be kept in mind:

**ANTICIPATION OF SIZE OF ADENOMA:** The surgeon may anticipate the probable size of a parathyroid adenoma by study of the abnormal physiology of the patient. We know of no clue as to whether an adenoma or primary hyperplasia will be encountered. The size of an adenoma is, however, roughly

proportional to the elevation of the blood serum calcium. If the elevation is minimal, with a level of 11 to 12 mg., and with a lowered blood phosphorus, the surgeon should realize that any adenoma will be small and may be hard to find. If the blood calcium is 14 mg., the problem is much easier for the tumor should weigh one-half or more grams. If the blood calcium is 15 mg., or above, the tumor may be large enough to palpate or to displace other organs and may be discovered rapidly. The converse is true; if a small adenoma is identified in a patient with a moderate or high elevation of the blood calcium level, a second adenoma exists and should be looked for.

The weight of the glands in primary hyperplasia has not borne such a constant relation to the blood calcium level; variations in the size of the glands in the same patient have been considerable.

The significance of the ability to anticipate the size of a possible adenoma is revealed in still another way. If a large parathyroid mass is encountered in a case with a mild degree of the disease (only slightly elevated blood calcium level), it is probable that the surgeon is not dealing with adenoma but with primary hyperplasia. The gland should, therefore, be inspected for the other characteristics of hyperplasia and the blood supply not damaged, for this may be the gland most favorably situated for subtotal resection.

**MULTIPLE ADENOMATA:** Four of the 54 cases of hyperparathyroidism due to adenoma, in this hospital's series, have each had two adenomata. In two cases, both adenomata were disclosed at the first operation. In the third, a minute adenoma was overlooked at the first operation when the larger adenoma was removed; residual disease required a secondary operation. In the fourth case, the disease was completely relieved for four years after the removal of the first adenoma. In the fifth year, the signs of a mild recurrence appeared and, at a second operation, a small adenoma was found. There are, in addition, two other cases in which one adenoma has already been removed, with a mild degree of the disease, presumably the result of a second adenoma. In one of these the disease was completely relieved for a period of more than two years after the first operation; in the other, there has been continuous disease since the removal of the first adenoma.

From these statistics, therefore, based on the incidence in this series of 54 cases, one would expect that approximately one case in ten of hyperparathyroidism due to adenoma will have more than one adenoma present. The criteria for seeking a second adenoma must be weighed by the surgeon. The surest way of excluding a second adenoma would be to isolate all four glands at the initial operation and, perforce, this may be necessary since one adenoma may not be discovered until after the three uninvolved glands.

It would be unwise, however, to prolong the operation unnecessarily in the majority for the exception. The principles which guide us in making the decision to seek a second adenoma at the same operation in which one adenoma and not all four glands have been found, are as follows:

The size of the adenoma in proportion to the degree of the disease is pri-

mary in importance (see page 720, Anticipation of Size of Adenoma). Since this proportion is only approximate, other considerations enter in.

If an adenoma, the adequacy of the size of which is debatable, is uncovered on the first side of the neck explored, it is wise to look for the second gland on that side. If this gland turns out to be uninvolved, it is reasonable to stop with resection of this single adenoma, anticipating that the disease will be relieved. If disease persists, the other side can be explored unhampered by scar tissue and with the knowledge that another tumor must exist. If both sides of the neck had to be explored to find an initial and probably inadequate adenoma, a second should be sought and a complete first-stage operation performed if necessary. Scar tissue makes reexposure so difficult that no field should be closed until it has been completely searched. Having failed to find the second adenoma at the first stage, the second stage will be indicated.

**USES OF EXPOSED UNINVOLVED GLANDS:** Scrutiny of an uninvolved gland exposed during the course of an operation may yield much information of service in directing the surgeon's further attack.

*Size and Shape:* In mild cases, the adenoma may be so small that it is embedded within a capsule of normal parathyroid tissue. Even though wide variations occur among normal glands, comparison of the size and shape of this gland with those of other apparently uninvolved glands may yield the only clue to the presence of the adenoma.

*Color:* In a gland of normal size and shape, a color yellower than expected tends to confirm the presence of an adenoma in another gland. A normal color of a gland slightly larger than normal suggests either that it hides an adenoma beneath the surface or is a secondary hyperplastic gland.

*Symmetry of Position:* In about 80 per cent of patients, the corresponding parathyroid glands occupy symmetrical positions in the two sides of the neck. If the first gland exposed is normal, it may be more efficient to proceed immediately to the symmetrical position on the other side rather than to prolong the search on the same side for the other gland of which there is no definite clue.

*Parathyroid III or IV:* As soon as a normal parathyroid is identified, it should be decided whether it is an upper or lower gland. If it is an upper (IV), any further dissection on that side should be below it; if it is a lower (III), presumably the upper will be higher. Accurate decision may be impossible when the gland lies in the branches of the inferior thyroid artery but careful search for the origin of the gland's arterial supply may furnish the lead. As pointed out above, under *Exploration Defined by Thymus*, the presence of any thymic tissue in proximity identifies it as a lower gland even if in an upper position.

*Exclusion of Hyperplasia:* The finding of one normal gland excludes primary hyperplasia. This simplifies the problem, for although it may be necessary to identify other normal glands if the adenoma is smaller than expected, in the majority of cases it will not be necessary to identify all parathyroid tissue.

**HYPERPLASIA:** Primary hyperplasia of all parathyroid tissue must be ex-



cluded when an enlarged parathyroid gland has been uncovered. If the gross characteristics are not sufficiently clear for identification and no other gland has been found for comparison, a piece should be removed and examined by frozen-section. The surgeon should not close until the decision in regard to the pathologic type of the disease is definite.

**IDENTIFICATION OF GLANDS BY BIOPSY:** If in doubt whether a piece of tissue is parathyroid, a specimen should be removed for biopsy. *Under no circumstances should the tissue be resected until it is proven an abnormal gland.* Eight surgeons, operating upon patients later sent to us for secondary exploration, removed tissue about which they were undecided. Some avowedly removed what they considered to be normal parathyroid glands. In each of three of the patients two normal parathyroids were actually removed. In these patients, had the adenoma, when found, been resected in entirety, only one normal gland at most would have been left to maintain parathyroid function. Since the viability of this remaining gland might have been jeopardized by operative trauma, if it was not unwittingly excised, a subtotal resection of the tumor was necessary. Since the removal of a small piece for biopsy by frozen-section is simple and a trained pathologist's report dependable, the procedure should be resorted to more frequently.

**SUPERNUMERARY GLANDS:** The possibility of more than four parathyroid glands in one individual menaces the surgeon's peace of mind. Although the text-books of anatomy definitely give four as the normal number of glands, pathologists have described as many as seven in a given individual; many authors have found less than four. The adequacy of the search is always open to question when less than four have been found. No one man has made a sufficient number of extensive dissections to show the real incidence of more than four glands in one individual. Embryologists are agreed that supernumerary glands can occur just as there may be detached remnants of thyroid or thymus in the neck.

In a small series of dissections, the author has encountered five normal glands twice. In one patient with hyperthyroidism, he has uncovered three normal glands on one side, proven by biopsy. From the practical point of view in dealing with hyperparathyroidism this single operative and limited dissection experience must be considered fortuitous. A working plan has been developed. If four normal glands, proven by biopsy, are isolated in a patient with a borderline degree of hyperparathyroidism, and particularly if these glands are symmetrically placed in characteristic positions, no search is made for a possible fifth gland. If, on the other hand, the diagnosis is irrefutable, a further attempt should be made. If the diagnosis in the patient is in doubt and the glands are asymmetrically placed, a possibly asymmetric fifth gland should be sought. Other signs of irregularly developed glandular tissue, such as a pyramidal lobe of the thyroid or thymic rests, would strengthen this decision to look further.

**SUBTOTAL RESECTION:** Subtotal resection of the parathyroid tissue in primary hyperplasia is carried out on the same principle as subtotal thyroidec-

tomy for the hyperplasia of hyperthyroidism. There are also indications for subtotal resection of an adenoma, one of which also calls for less radical resection of primary hyperplastic tissue. A human being cannot survive total absence of parathyroid tissue with any comfort or safety in spite of the administration of the recently introduced A. T. 10. The indications for subtotal resection have been given in a previous article<sup>1</sup>; a new emphasis is given in the present review.

If a patient has had a previous parathyroid exploration and one or more normal glands have been removed, subtotal resection of an adenoma is indicated unless viable, uninvolved parathyroid tissue is definitely seen. Subtotal resection may be indicated, if a previous search has been made, even though no normal tissue was known to have been removed. If at the secondary operation dense scar tissue is found in the region where normal glands are most likely to occur, it is safer to assume that the uninvolved parathyroids have been damaged either by direct trauma or loss of blood supply. If pieces of tissue were cut out for examination, or particularly if a subtotal thyroidectomy was done in the hope of finding parathyroid tissue within the thyroid substance, a subtotal resection should be weighed.

Subtotal resection of an adenoma or less radical subtotal resection of primary hyperplasia is indicated if tetany of the recalcification period is anticipated. In patients with extensive bone disease, secondary to hyperparathyroidism, severe low calcium tetany may follow correction of the primary disease. This tetany is due to the rapid absorption of calcium by the bones. Preoperatively, it may be predicted if the phosphatase of the serum is ten Bodansky units or greater.

The nature of this tetany of the recalcification period is not completely understood. The disordered metabolism resulting in the decrease of blood calcium is different from that in hypoparathyroidism. First, the serum phosphorus level is low instead of high. Already low due to the hyperparathyroidism, it descends further during the 48 hours after operation, rising to the low preoperative level in the course of the first postoperative week, and to normal as recalcification is completed. Second, the phosphatase, already elevated, rises precipitously after operation (during the first 48 hours there may be a transient fall). As the skeleton recalcifies, the phosphatase falls gradually to normal. In patients with severely depleted bones, this process may require more than a year in spite of a huge daily intake of calcium and phosphorus. During this long period, tetany remains latent.

The phosphatase level of the blood serum is believed to be proportionate to the number of osteoblastic cells ready to form bone. In the presence of an excess of parathyroid hormone, these cells are unable to work to capacity. The change in parathyroid function following resection of an adenoma apparently releases them much as a trigger fires a gun. Their rapid absorption of calcium results in the tetany. It may be that subtotal resection is not the best method of slowing up the discharge of this tetanic gun.

The possible occurrence of carcinoma in the remnant of the parathyroid

adenoma might be considered as a contraindication to subtotal resection. In only one of our nine cases in which a subtotal resection of an adenoma has been done, have we had to remove the remnant for residual hyperparathyroidism. In none of the 58 adenomata seen at this hospital has there been any microscopic evidence of malignant degeneration. The report<sup>13</sup> of carcinoma in a gland giving rise to hyperparathyroidism is not beyond question. Carcinoma of the parathyroid is a rare disease; in the cases reported no hyperfunction is proven. The possibility of eventual carcinoma should not rule out subtotal resection when life-endangering tetany threatens.

#### ILLUSTRATIVE CASE HISTORIES

The following case revealed a parathyroid adenoma in the anterior mediastinum, impossible to reach by fingers introduced through a collar incision in the neck:

**Case 50.**—*Mediastinal Adenoma Beyond Reach from the Neck:* A woman, age 26, was treated in a hospital in Hartford, Conn., two years before entry. First, a calculus was removed from the right ureter, then the left kidney was removed because of stones and infection. Following this, a diagnosis of hyperparathyroidism was made on the basis of the blood findings. Exploration of the neck and thyroid regions disclosed three enlarged glands, felt to be consistent with hypertrophy. Specimens were removed for biopsy; normal parathyroid glands were reported. The metabolic signs of hyperparathyroidism continued and the patient was referred to this hospital.

Intravenous pyelograms pictured calcification in the right kidney and slight hydro-nephrosis. There was no demonstrable bone disease roentgenologically. There was hypercalcinuria, a blood calcium level of 13.6 mg., phosphorus of 2.4 mg., phosphatase of 4.2 units.

**Operation.**—Because of the gross diagnosis of hypertrophy made at the previous operation, the neck was reexplored. The thyroid region was searched. A remnant of one of the glands previously exposed was identified, a specimen removed for biopsy, and reported normal. Because of its nodular character, the left thyroid lobe was subtotally resected; sectioned at the operating table, but no parathyroid tissue was found. The entire neck region and posterior mediastinum were explored. Then the anterior mediastinum was entered by blunt finger dissection. A normal thymus gland was identified and the upper portion was teased out; no parathyroid tissue was found in it and none had been felt near it. Tissue could be felt in the anterior mediastinum at the tip of the finger, and it was realized that more thymus was left in the chest.

During such a blunt, blind search in the anterior mediastinum there is inevitably considerable motion of air in and out of the chest, and its occurrence at this operation failed to cause concern. The patient died two hours after operation of a bilateral partial pneumothorax. By the blunt dissection, small openings had been torn into the pleural cavities. Postmortem examination confirmed the presence of further thymus tissue lying in front of the ascending aorta, and at the very bottom, poking its nose out of the thymic capsule, lay the parathyroid adenoma. The adenoma lay just in front of the upper portion of the right auricle, between the upper anterior pericardium and the sternum. It was fully two inches below the reach of fingers inserted at the notch of the manubrium (Fig. 11).

**COMMENT.**—This parathyroid adenoma was in the lowest position of any we have found, and lower than any parathyroid gland we have seen reported in the literature. The experience with this patient demonstrates not only the danger of blunt and blind dissection in the chest but also that parathyroids

may be beyond reach; it has been responsible for our considered return to direct exploration of the anterior mediastinum through a divided sternum.

The following case illustrates the wisdom of exploring the anterior mediastinum under direct vision. The adenoma was not felt although touched by fingers inserted from the incision in the neck. Its position was not disclosed until the second-stage operation:

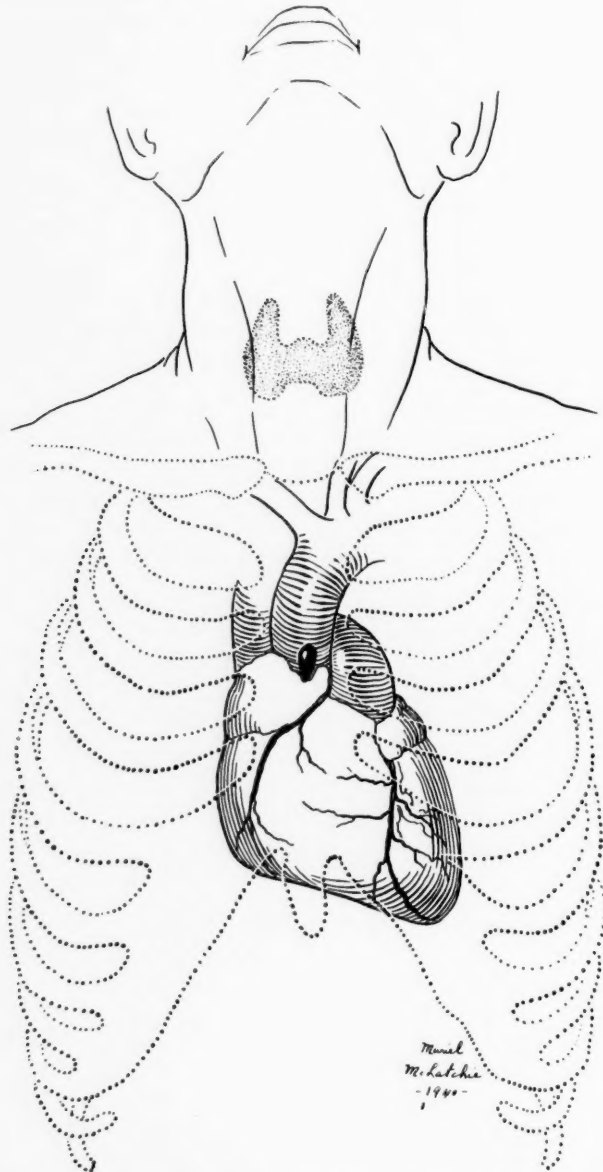


FIG. 11.—Position of parathyroid adenoma found at autopsy in Case 50. The adenoma lay at the lower end of the thymus within the thymic capsule and was a good two inches beyond the reach of fingers introduced through the neck incision.

**Case 55.**—*Futility of Blind Exploration of Anterior Mediastinum:* A woman, age 54, eight years before entry underwent a pelvic repair operation. A backache which was unrelieved by the operation was later diagnosed sacro-iliac arthritis. Four years later, during a gastro-intestinal series, kidney stones were discovered, and after another year one kidney "full of stones" was removed. It was not until 18 months before entry, when she was studied for various skeletal aches, that hyperparathyroidism was diagnosed. A parathyroid exploration was undertaken in New York, N. Y. The neck region was explored but only one parathyroid, presumably a normal one "at the right lower pole of the thyroid," was disclosed. Because of increasing skeletal pains and continued hypercalcinuria, the patient was referred to this hospital.

Mild generalized decalcification was demonstrated. The blood serum calcium averaged 15.5 mg., the phosphorus 2.1 mg., and the phosphatase 7 units. There was a high concentration of calcium in the urine.

*Operation.*—Since the surgeon had been able to expose only one possible parathyroid gland at the previous operation, reexploration of the neck was indicated.

*First Stage.*—November 23, 1940: The areas covered at the previous operation were clearly delineated by dense scar tissue; a complete exploration of neck and posterior mediastinum was accomplished and no parathyroid adenoma was found. In an effort to avoid a third operation the anterior portion of the superior mediastinum was explored blindly with fingers; no tumor was felt.

*Second Stage.*—December 5, 1940: After division of the sternum, a long, thin thymic remnant was easily identified. It was dissected upwards to within 1 cm. of the left innominate, where dense tissue reaction from the recent blind exploration was encountered. No parathyroid tissue was seen within the free portion of the thymus. Other portions of the mediastinum were, therefore, explored. When no tumor was found the scarred area was returned to as last resort. As the thymus was followed up into the area where fingers had felt before, a parathyroid adenoma, measuring  $1.8 \times 0.8 \times 0.5$  cm. and weighing 0.4 Gm., was found within the thymic capsule, lying behind the inferior margin of the left innominate vein. Figures 8 through 10 are photographs taken at the operation of this patient.

Removal of the entire adenoma has resulted in prompt relief of the patient's symptoms.

**COMMENT.**—The adenoma was undoubtedly touched at the first-stage operation. Although of moderate size, it was not felt as a distinct body because of its soft character and its inclusion within a tissue of nearly the same consistency and its position near a large collapsible vein. By yielding to temptation at the first stage the second was made much harder.

In the following case, the thymus gland served as a guide to the prompt discovery of a parathyroid adenoma embedded in the scar tissue of the previous explorations:

**Case 57.**—*Area of Exploration Defined by Thymus:* A woman, age 30, noticed the onset of bone pains seven years ago. During the course of these years the pains spread to her whole body and the severity increased. During the last eight months she was bedridden.

Three and one-half years ago, at two operations in a hospital in New Haven, Conn., epulis tumors were removed. Three years ago, in a second New Haven hospital, the diagnosis of hyperparathyroidism was made. Two parathyroid explorations were performed. At the first, the neck was explored and "a parathyroid at the anterior surface of the upper pole was identified and removed"; pathologic section showed it to be a lymph node. At the second, the sternum was divided with rongeurs and the anterior mediastinum explored; no parathyroid tumor was found.



Two years ago, in a third New Haven hospital, a second exploration of the neck was made; subtotal thyroidectomy failed to reveal any parathyroid tissue. Six months ago, at a hospital in Boston, Mass., a third exploration of the neck was made; the available portions of the mediastinum were searched. After this fourth unsuccessful operation, roentgenotherapy was administered to neck and mediastinum.

Because the disease had progressed relentlessly, she was referred to the Massachusetts General Hospital. The skeleton showed an extreme degree of involvement with several huge giant cell tumors. The left ureter was blocked by a large stone. She had a severe anemia, in spite of a 4 per cent reticulocyte count. Her blood volume was increased 35 per cent above normal. The blood calcium was 14.5 mg. and phosphorus 2.2 mg.

*Operation.—Second Stage:* Because of the three previous attempts we excluded generalized hyperplasia and thought the existence of a tumor in the neck or posterior mediastinum unlikely. An adenoma was presumably to be found in the anterior mediastinum lower than the area previously searched. It was, therefore, decided to explore first the region of the lower ascending aorta and pericardium. The sternum was divided into both interspaces and the aorta identified. The lower end of clearly defined thymus was exposed; the margins led upward into the scar tissue of the previous operation. Because it was unlikely that parathyroid tissue would exist below thymus, it was decided to follow the thymus through the scar tissue in spite of the previous search. As the thymus was freed upward, a large adenoma was seen lying against the pleura on the left side. The adenoma lay outside the thymus but in close proximity; it was posterior to the plane of the thymus, between pleura and upper ascending aorta. The anterior and medial surfaces were scarred, showing that previous dissection had come near it. The main arterial supply entered the gland near the bottom, coming from vessels along the pleura and lung root. The largest vein emptied upward into the innominate vein.

The adenoma was subtotally resected because of the possible damage produced by the previous explorations and thyroidectomy, and also because of the extensive bone disease. The remnant was swung anteriorly behind the manubrium on the venous pedicle. The thymus gland was left intact.

In this patient, prolonged search was obviated by scrutiny of the neighborhood of the thymus.

*Discussion.*—The first patient in whom a parathyroid adenoma was found in the anterior mediastinum by the direct approach through the sternum was Case 6 of this series. It was this patient's seventh operation seeking the tumor.<sup>3,4\*</sup> One week later, in another patient, we removed a parathyroid adenoma from a similar position by teasing it out with fingers introduced through the neck incision. Both tumors lay opposite the second intercostal space, and, in retrospect, it was believed that the first tumor could have been pulled out by the same procedure had its position been accurately known. Since then, two more tumors hidden from view have been fished out of the anterior mediastinum, and in the last publication on the surgical problem from this hospital<sup>4</sup> it was stated that "splitting of the sternum to afford a direct visual approach to the anterior mediastinum is a procedure that will rarely be required."

Since publication of this article, experience has modified this point of view: First, a patient, not included in the series of proven cases, suspected

\* Gordon-Taylor and Handley<sup>14</sup> have also reported the removal of a parathyroid tumor by a transsternal approach.

of having a mild degree of hyperparathyroidism was operated upon. The entire neck and posterior mediastinal regions were explored; three asymmetrically placed normal parathyroids, but no adenoma, were isolated. The anterior mediastinum was searched by palpation with fingers. Nothing further was found and the fallacy of this blind procedure was then appreciated. If this patient indeed had the disease, the tumor would have been small and, therefore, not palpable.\*

In addition, there are the two patients mentioned above under Multiple Adenomata (page 721) who presumably have a second adenoma (mild hyperparathyroidism remains following the removal of the one adenoma), and who have had their anterior mediastinum explored digitally.† Finally, there is Case 50, with the adenoma which was totally inaccessible. With this one definite and three probable failures (to recover a parathyroid tumor from the anterior mediastinum *via* the neck incision) to our debit, a reevaluation of the sternal-splitting operation was imperative.

The direct approach to the anterior mediastinum has now been employed on five patients. The adenomata of three of the nine patients with previous unsuccessful operations were found by this approach; in only one of these, Case 57, did we proceed directly to the thorax without first reexploring the neck. In the fourth patient, Case 54, the use of the second-stage followed the first-stage as outlined in this paper.

The fifth time the anterior mediastinum has been explored through a divided sternum was in a boy, age 14, in whom hyperparathyroidism was excluded by operation. Acute atrophy of bone had simulated hyperparathyroidism. His case is reported elsewhere.<sup>15</sup>

The illegitimate employment of the sternal-splitting operation will raise the operative mortality of hyperparathyroidism. The complications of opening the thorax are greater than those of exploring the neck but not greater than those of attempting to explore the thorax from the neck. If the anterior mediastinum must be explored, it is as safe to do so directly at a second operation, and this operation will be successful. The only way to prevent the increase in the mortality rate of the surgery of hyperparathyroidism is to make certain by an adequate first-stage operation (neck and posterior mediastinum) that the second-stage (anterior mediastinum) is essential.

#### SUMMARY

The problem of the surgery of hyperparathyroidism resolves itself into training of the eye, understanding the abnormal physiology of parathyroid glands and recognition of their widespread distribution.

\* Since no further ureteral stones have appeared and the metabolic changes remain questionably abnormal, direct exploration of the anterior mediastinum has not been advised and the nature of this patient's fourth gland is not known.

† One of the two patients, Case 11, had developed carcinoma of the thyroid between the primary and secondary operations. The other, Case 40, has had to undergo a gastrectomy since his parathyroid operation. Exploration of his anterior mediastinum is contemplated.

The incidence of enlarged parathyroid glands in the mediastinum in 60 proven cases, from the Massachusetts General Hospital, is reported.

The difficulties in discovering these glands in the anterior mediastinum are reviewed; blind dissection with fingers is uncertain and as hazardous as the direct approach by splitting the sternum.

The operative plan as employed at present at this hospital is described in detail. The search is divided into two stages. In the first, the neck and posterior mediastinum are explored. In the second, the anterior mediastinum is opened to dissection under direct visual control by splitting the sternum. This second-stage must be reserved until after an adequate first-stage operation.

The large number of cases of hyperparathyroidism diagnosed at the Massachusetts General Hospital speaks for the tradition of metabolic research of our medical colleagues. The success in proving the diagnosis and benefiting the patient is a result of the versatility of Dr. Edward D. Churchill's surgical point of view. The author is indebted to him not only for sharing the operative assignment of parathyroid disease but also for his criticism.

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DISCUSSION.—DR. FRANK H. LAHEY (Boston, Mass.): I wrote to the authors, when they invited me to discuss this paper, that I would only accept the invitation with the statement that I had not had a large experience with this problem. On the other hand, we have dealt with some of these intrathoracic parathyroid adenomata. It is an interesting subject. It is one that needs frequent discussion, and it is particularly interesting to hear this paper from the Massachusetts General Hospital, where so much pioneer work has been done on this subject.

I am sure that Doctor Cope will not feel offended if I reiterate what he has already said, that this represents the combined efforts of the medical men at the Massachusetts General Hospital, who have been interested in metabolic disease there, and the surgeons, and all of us who have anything to do with hyperparathyroidism must feel a deep sense of obligation to the men in the Massachusetts General Hospital who have done this work. They have done the pioneer work in this country to establish this disease on a sound basis.

Figure 1 shows a patient with an intrathoracic parathyroid adenoma which I removed; and demonstrates the degree of chest collapse and round back which can develop in these large parathyroid adenomata. It is interesting that Doctor Cope and his group have demonstrated the relationship of the intensity of the disease to the size of the tumor. Figure 2 is a roentgenogram of this patient, with shadows marked out, the lower shadow being the arch of the aorta, and the upper shadow the adenoma in the mediastinum. Note the amount of vertebral body collapse. Figure 3 shows about two-thirds of the tumor removed from the mediastinum.

On the other hand, Figure 4 is a roentgenogram showing a mediastinal adenoma which has become cystic, which probably never produced any symptoms. That was removed last year, without difficulty, from the mediastinum.

So we have at least the problem that we can have some of these adenomata not producing the degree of decalcification that goes with the usual case.

One of the problems with which we have had to deal is the intrathyroid parathyroid adenoma. We have found three intrathyroid parathyroid adenomata and, as the author

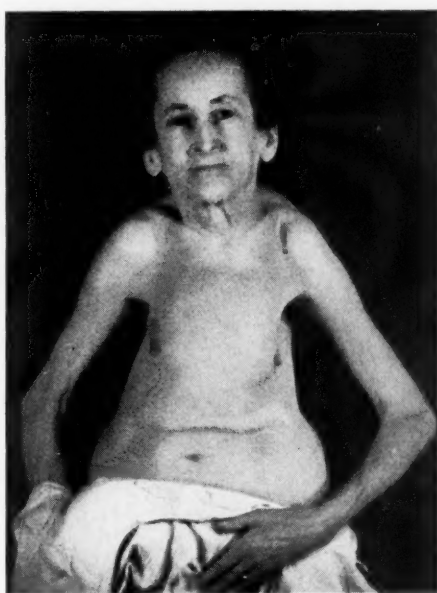


FIG. 1.

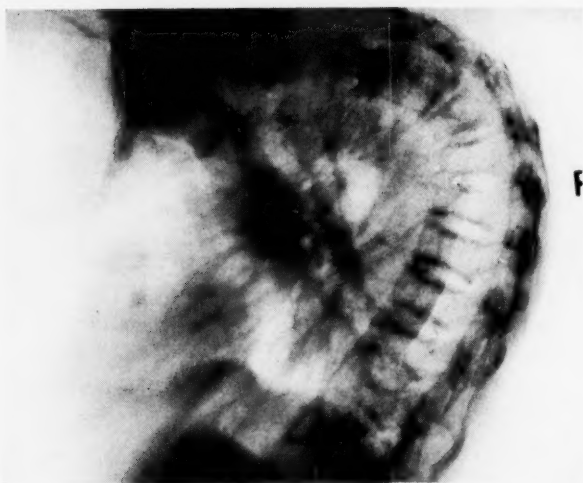


FIG. 2.



FIG. 3.



FIG. 4.

states in his paper, the parathyroid adenoma which is apt to be intrathyroid due to the fact that it rests against the side of the larynx, where the upper lobe presses on the larynx, is the superior parathyroid.

Now, I would like to say just a few words for those general surgeons who do not deal with these cases in large numbers. In the paper, there is stressed the fact that there should not be removal of normal parathyroids. We have had to operate on some of these, in which two of the parathyroids have been removed, and so it presents a very serious problem. One should learn, in dealing with thyroids, what normal parathyroids look like. Since we have transplanted 300 microscopically proven parathyroids in the course of thyroidectomies, we have acquired a considerable knowledge of at least the normal location and the appearance of normal parathyroids.

The successful demonstration of parathyroid adenomata will have to do with good exposure, dry fields, good lights, experience with what a normal parathyroid looks like, and mobilization of the thyroid gland. You must, if you look for these parathyroids, tie all the venous connections of the parathyroid gland, which are to the internal jugular. You must then elevate the thyroid gland out of its bed, ligate the superior thyroid



## HYPERPARATHYROIDISM

vessels, and detach the upper pole from the larynx, so the gland is adherent only by its attachment to the trachea. You must palpate through-and-through, and, following this, you must, at a later date, in all probability expose the mediastinum. We have exposed the mediastinum in three cases. A very satisfactory way, after splitting the sternum, is to insert the right-angle retractor in the split mediastinum, and then turn it into the longitudinal position, which spreads the manubrium, so the mediastinum is exposed.

I cannot close this discussion without saying what an excellent paper this is. I have read it over thoroughly, and I said to the author that no 15-minute presentation of this paper could do it justice. When you read it, I think you will all agree that it will play a very great part in later making easier for all of us the discovery of some of these adenomata of the parathyroid which, up to now, have been overlooked.

DR. EDWARD D. CHURCHILL (Boston): In the natural eagerness to find the parathyroid tumor, the importance of identification of the normal glands must not be forgotten. To put the matter simply, don't go afield looking for a lost sheep until you have counted the ones that are safe in the fold. As soon as the presence of a large prolonged search directed toward finding normal parathyroids. Carefully observe and record the positions of the normal glands. Then, by exclusion, it may be possible to go directly to the site of the missing parathyroid adenoma.

DR. OLIVER COPE (Boston, closing): I might emphasize just one point: a distinction should be drawn between a normal gland and an uninvolved gland in a person who has hyperparathyroidism due to adenoma. Doctor Churchill has called attention to the advisability of identifying normal glands. One of the reasons it has been hard to find so-called "normal glands" when looking for an adenoma, is that due to atrophy of disuse they have lost their normal color and are smaller. These atrophic, uninvolved glands are more difficult to distinguish than the normal glands encountered during the course of a thyroidectomy.

## OBSERVATIONS ON INTRATHORACIC NEOPLASMS\*

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INTRATHORACIC NEOPLASMS are great dissimulators. Whereas, their usual symptoms are cough, sputum that may be blood-tinged, dyspnea and pain, a surprisingly large proportion of patients with intrathoracic neoplasms present a combination of symptoms, physical signs, and even roentgenographic shadows that initially suggests virtually any of the commonplace diseases of the chest. I have recently seen patients with bronchogenic carcinoma who were variously treated for pulmonary tuberculosis, cardiac disease with pulmonary embolism, asthma, chronic bronchitis, pulmonary abscess and delayed resolution of pneumonia for from one to 16 months before the true diagnosis was suspected and made. A patient with a primary sarcoma of the lung, which was first observed as a silent circumscribed shadow, was advised by a well-known internist to have a check-up roentgenologic examination in from three to six months; at four months the shadow had not increased in size and a later roentgenogram was advised; the patient had this made one year later, at which time the tumor filled nearly three-quarters of his hemithorax (Fig. 3). A patient with an intrathoracic spindle cell sarcoma, that overlapped the left border of the heart, was treated by a heart specialist with digitalis for 13 months for cardiac enlargement and a murmur that suggested mitral stenosis. A patient I have recently seen with a neurofibroma was treated for diaphragmatic hernia for six months, and another was treated for scoliosis with low back pain for 15 months. Many of the tragic consequences that such mistakes entail may be avoided by a critical examination of some of the diagnostic errors that are likely to lead to mistaken diagnoses. Space will not, however, permit a complete discussion of those nonneoplastic lesions that may be mistaken for neoplasms.

In the present communication, I shall present chiefly those personal observations on intrathoracic neoplasms that have been made by my colleague, Cameron Haight, and myself, during a period of many years. Many of the statements I shall make, and advice I shall offer, are based on lessons we have learned from diagnostic and other errors we have made in meeting situations for the first time that have not been adequately described by others or that have been only incidentally mentioned in case reports. I shall not undertake, at this time, to present a systematic discussion of the diagnostic and technical surgical phases of the subject, as they have been well presented in the recent excellent monograph of Heuer and Andrus, in the text-books of Graham, Singer and Ballou, Sauerbruch, and Lilienthal, and in the articles

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of Harrington, Denk, and many others. I shall, in short, present here chiefly those observations that seem to me of great practical importance and that have not been discussed or sufficiently emphasized in previous publications.

An ordinary cold, influenza, pneumonia, bronchiectasis, or pulmonary abscess is often the first condition to attract attention to a thoracic illness in cases of neoplasm. Pressure upon the bronchi and lung by an intrapulmonary or extrapulmonary tumor in some way probably initiates the pulmonary infection in many cases. The error in failing to diagnose a neoplasm with reasonable promptness in such cases arises when the persistence of a customarily self-limited infection, or atypical developments in chronic infections, do not arouse sufficient suspicion to cause the physician to investigate the case further. The occurrence, the persistence or the aggravation of pain, dyspnea, or cough is especially suspicious of neoplasm in such cases.

Tuberculosis and asthma are frequently, and whooping cough is occasionally, mistakenly diagnosed in cases of intrathoracic neoplasm. Cough, blood-streaked sputum, fever, night sweats, fatigue, and pleural pain suggest tuberculosis, and the roentgenographic appearance of some cases of bronchogenic carcinoma may resemble atypical forms of tuberculosis, but the persistent absence of tubercle bacilli from the sputum should arouse a suspicion of tumor. The paroxysmal coughing that occurs in many cases of neoplasm may be mistaken for whooping cough. The asthmatoïd wheezing caused by intrabronchial growths or by extrabronchial pressure has been diagnosed as true asthma innumerable times. The confusion is promoted by the fact that, like neoplasms, asthma persists and often gradually becomes worse, and by the further fact that adrenalin and certain other drugs that relieve the attacks of asthma may also relieve the asthmatoïd wheezing produced by tumors through reduction in vascular congestion. Furthermore, an eosinophilia may occur with uncomplicated neoplasm.

Although pleural effusion occurs with some neoplasms, an encapsulated effusion or empyema, especially an interlobar one, is often diagnosed as the only lesion when no effusion whatever exists. The chance of a mistaken diagnosis of empyema is increased if the patient has fever, leukocytosis, night sweats, and loss of weight, as he may have with some forms of uncomplicated neoplasm, whether benign or malignant. Although the physical signs may be the same in pleural fluid and neoplasm, the history and roentgenologic findings in a huge majority of cases of neoplasm are sufficiently characteristic to lead to a correct differential diagnosis.

Among the manifestations of cardiocirculatory disease that may be simulated by intrathoracic neoplasms are anginal pain, cardiac murmurs (from direct pressure upon, or rotation of, the heart), abnormal electrocardiogram from direct invasion of the cardiac wall by a malignant neoplasm, apparent cardiac enlargement, palpitation, dyspnea, cyanosis, venous dilatation (usually, however, confined to the supply beds of either the superior or inferior vena cava), apparent enlargement of the liver (from depression by a large intrathoracic tumor), and aneurysm. The differential diagnosis

between an aortic aneurysm and a mediastinal neoplasm is at times very difficult because their roentgenographic shape, size, and position may be identical, because a patient with a neoplasm may happen to have a positive Kahn reaction, and because the fluoroscopic and kymographic determination of whether a mediastinal mass has expansile or only transmitted pulsation may be impossible. I have deliberately explored two such cases, in which the clinical situation was desperate, believing them to be aneurysms (which they were), because there was a small but reasonable chance that a removable

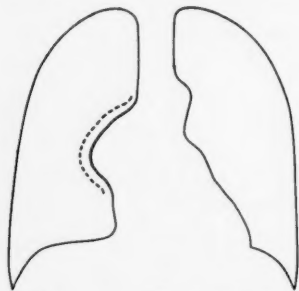


FIG. 1. — Fluoroscopically, transmitted pulsation of a tumor may be mistaken for expansile pulsation because the outward thrust of a circular or irregular tumor by transmitted pulsation may create the optical illusion of expansile pulsation.

neoplasm might be found. In another case—that of a nonsyphilitic, arteriosclerotic man with a circumscribed nonpulsating tumor lying snugly in the lower left costovertebral gutter—I operated expecting to find a neurofibroma but found an aneurysm instead. On the other hand, I have removed a solid mediastinal neoplasm that was attached to the aortic arch, and which an excellent roentgenologist stated had expansile pulsation (Fig. 1).

Arthritis, usually accompanied by hypertrophic pulmonary osteo-arthritis, not rarely occurs early in the course of the thoracic symptoms arising from intrathoracic neoplasms. Willard Van Hazel has recently reported five cases of malignant tumor and two cases of benign tumor in which the sudden onset of arthritic symptoms and joint changes occurred from one month to one year before any thoracic symptoms of the neoplasm appeared. In several of these cases, the arthritic symptoms and signs disappeared within a day or so of the removal of the tumors. While I have seen many cases in which arthritic symptoms and clubbed fingers and toes were apparently a part of the neoplasm syndrome, I have seen only one in which there was sudden relief of the arthritic symptoms following the removal of the tumor, a 1,760 Gm. spindle cell myxofibrosarcoma. All the teeth of this patient had been extracted for his presumed arthritis.

Pain in the chest, neck, arms, or abdomen is one of the most valuable of all symptoms in suggesting the possible presence of an intrathoracic neoplasm. Pain may first occur with some form of pulmonary infection and for weeks or months may be intermittent in character. The mistake is frequently made of attributing a progressive thoracic pain to a simple pleurisy, intercostal neuralgia, or spinal arthritis, and of attributing pain in the neck and shoulder region to arthritis or diaphragmatic pleurisy, in the arm to angina pectoris or neuralgia, and in the abdomen to gallbladder disease, gastric or duodenal ulcer, or other abdominal lesion.

When a diagnosis of an intrathoracic neoplasm has been made, the important questions arise as to whether the tumor is benign or malignant and, if malignant, whether it is probably completely removable. An accurate

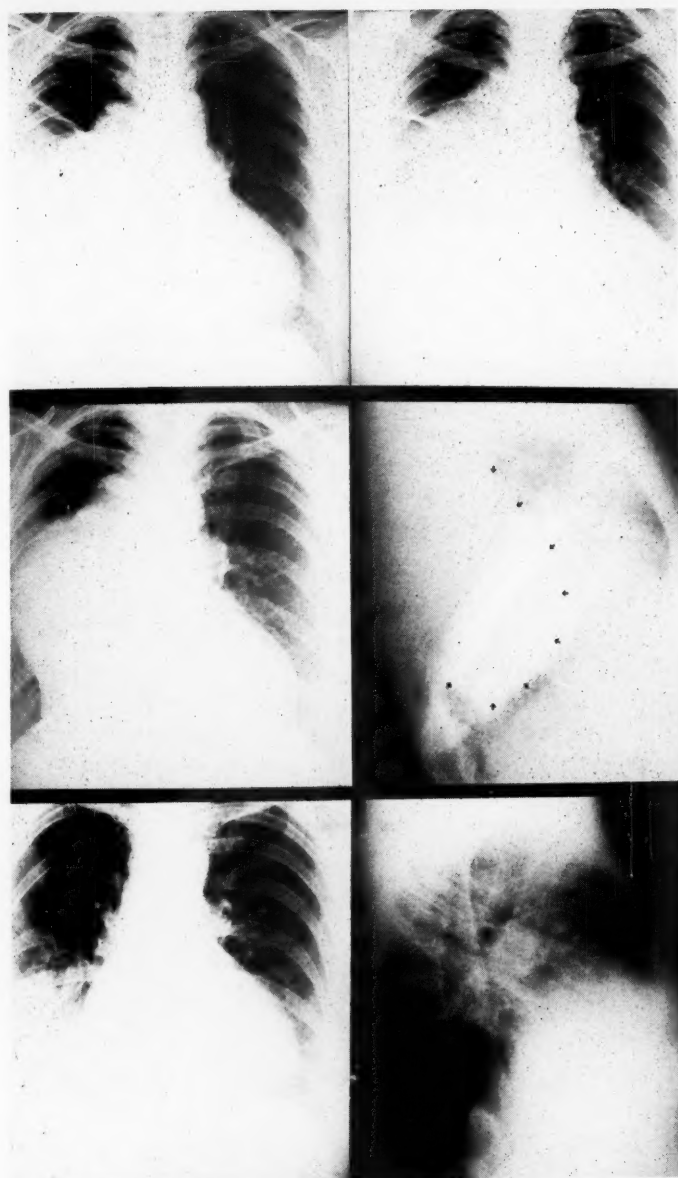


FIG. 2.—In 1935, a female, age 54, with hypertension, had an acute upper respiratory infection accompanied by sudden dyspnea, cough without sputum, and fever for only two days. 1,000 cc. of clear, straw-colored pleural fluid were aspirated and then the roentgenogram showed a tumor. Top row, left, 2-23-35, before aspiration; right, 3-4-35, after aspiration.

During the next five years the patient had fairly good health except for some dyspnea, a sensation of tightness in the chest, and several brief attacks of pleurisy. She had no cough, sputum or hemoptysis. Roentgenograms in 1937 showed an increase in the growth of the tumor. The postero-anterior and lateral roentgenograms of February, 1940, are reproduced in the middle row. The patient was rejected for surgical treatment by a well-known clinic in February, 1940, because of the risk of operation in a patient, age 59, with hypertension; the long duration of the disease; and the few troublesome symptoms.

She was referred to me by Dr. R. L. Pott, of Grand Rapids, in March, 1940. I advised operation because of the danger to the already overworked heart from direct pressure by the increasing size of the tumor, because of the danger of malignancy; and because of the probability of the development of severe pain. After taking a 1,200 calory diet for three and a half months, the patient lost 18 pounds, and the blood pressure dropped from 210/100 to 170/90.

The tumor, which was reported by Dr. C. V. Weller as a rather cellular xanthofibroma with numerous foam cells, not sufficiently cellular to be considered sarcomatous but which might be expected to recur if not completely removed, was completely removed on 7-25-40. There was only mild, brief postoperative shock, and the patient left the hospital 20 days after operation, with a blood pressure of from 120/60 to 142/74, with a pulse of from 80 to 90. For several months her systolic blood pressure was about 130 but when last seen at the end of October, 1940, was about 205. The patient then had no complaints except slight dyspnea and tightness in the chest, and was doing light housekeeping without difficulty. The bottom row of roentgenograms were made on 3-5-41, seven months after operation.



preoperative pathologic diagnosis of intrathoracic neoplasms, apart from esophageal carcinomata and those bronchogenic carcinomata that can be biopsied endoscopically, and those neoplasms that have infiltrated the thoracic wall or have metastasized to a site from which a biopsy specimen may be obtained, is virtually impossible. Exception may be taken to this statement on the ground that an exact diagnosis can frequently be made from a needle aspiration biopsy specimen. I advise against aspiration biopsy in any but exceptional circumstances because (1) the preoperative determination of the cell type and of benignancy or malignancy does not determine operability; (2) the introduction of a large needle into a tumor may cause hemorrhage inside or outside it, may cause a cyst to rupture or to spill possibly infected contents, may produce a cerebral embolism or, if the tumor is malignant, may produce an implantation metastasis in the needle track of the thoracic wall; (3) the introduction of a large needle into an intrapulmonary tumor across a pleural cavity that may not have been obliterated by adhesions may cause pyogenic organisms from the lung to infect the pleural cavity, thereby greatly reducing the chance of a successful removal of the tumor.

As many benign neoplasms are potentially malignant and as a reasonably large proportion of malignant tumors can be removed completely, virtually every case of intrathoracic tumor should be promptly explored surgically: (1) If there is no evidence of metastasis or irremovable invasion of the adjacent thoracic wall; (2) if the patient's general condition does not contraindicate the operation; and (3) if the tumor is not a lymphoblastoma. Mediastinal tumors with a circumscribed border are especially difficult to diagnose; lymphoblastoma, dermoid cyst or teratoma, aneurysm, mediastinal abscess, a mass of tuberculous nodes or of carcinomatous nodes of which the primary carcinomatous lesion may not have been discovered, fibroma, lipoma, thymoma, various forms of nonlymphoblastomatous sarcoma, and miscellaneous other neoplasms must be considered. When there is doubt as to the diagnosis, as there frequently is, and when an enlarged lymph node is not available for microscopic examination, the patient should be given a therapeutic test dose of deep roentgenotherapy in order to determine whether the response indicates the probable presence of a lymphoblastoma. I cannot emphasize too strongly that, with rare exceptions which may be disregarded, this is the only proper use of roentgenotherapy as a diagnostic or therapeutic measure in possibly operable thoracic neoplasms. I have seen a number of patients with both intrapulmonary and extrapulmonary malignant neoplasms who lost their lives because they were denied surgery at a time when their tumors were probably completely removable, merely because the tumors had temporarily decreased slightly in size as a result of roentgenotherapy. By these remarks I do not intend, of course, to deny the great palliative, temporary benefit that roentgenotherapy may bestow upon certain patients with inoperable intrathoracic neoplasms.

In the last paragraph, I stated that every intrathoracic neoplasm, with

certain exceptions, should be promptly explored surgically. While it is true that many benign and even some malignant tumors grow very slowly and can be safely removed after a long period of observation, it is equally true that a much larger number of tumor cases suffer seriously or fatally from the delay caused by a period of observation. Increasing experience has shown that many strictly circumscribed intrapulmonary and extrapulmonary tumors, which were formerly generally considered as benign, are malignant. If, therefore, circumscribed tumors are observed for one or more months in an effort to determine whether the rate of growth indicates benignancy or malignancy, the malignant tumors are likely to become inoperable because of metastases. The case shown in Figure 3 illustrates the fallacy of reliance upon rate of growth for the determination of benignancy or malignancy. Recently, I saw in consultation a patient who had had a small, well-circumscribed lesion in the lingular portion of the left lung which increased only slightly in size during an 18-month period of observation; during the last few months of observation an abscess formed in the lesion and obstructive bronchial symptoms finally led to a bronchoscopic diagnosis of carcinoma, which was then inoperable. As neoplasms that are actually benign often unexpectedly become malignant (perhaps after the termination of a period of observation designed to determine benignancy or malignancy), and as benign tumors may slowly or rapidly grow to enormous size, seriously impairing the function of the lungs and mediastinal organs, when the risk of their removal is many times greater than the risk of their removal when small, there is a real danger to life in delaying operation for benign tumors. Furthermore, the degenerating central portions of enlarging benign tumors, or the contents of dermoid or other cysts, may perforate into a bronchus, the tumors thereby becoming secondarily infected and densely adherent to their surroundings. The growth of neurofibromata arising in or near an intervertebral foramen, may proceed into the spinal canal, producing spinal cord paralysis.

If, as I believe, all benign and malignant neoplasms, with certain exceptions, should be promptly explored surgically, it follows that surgical exploration should be carried out for those wholly silent neoplasms that are accidentally discovered in the course of a routine physical examination (Fig. 3). They are as dangerous in the silent stage as in the symptomatic stage. If the tumor should be malignant, metastases may occur while the patient and physician are awaiting the possible occurrence of troublesome symptoms. Surgical removal is the only curative treatment of either benign or malignant neoplasms.

In the preceding paragraphs, emphasis has been placed upon the difficulty or impossibility of determining before operation in many cases whether a tumor is benign or malignant, and upon the importance of prompt operation unless metastasis or invasion of the thoracic wall indicates that the tumor is malignant and irremovable. Obviously, an effort should be made

to determine if such invasion or metastasis has occurred. Careful palpation for an enlarged cervical or axillary lymph node, the microscopic examination of which might show malignancy, has not rarely determined inoperability. The routine examination of the entire body, including the liver, spleen, kidneys, breasts, uterus, prostate, and testicles for possible primary or meta-

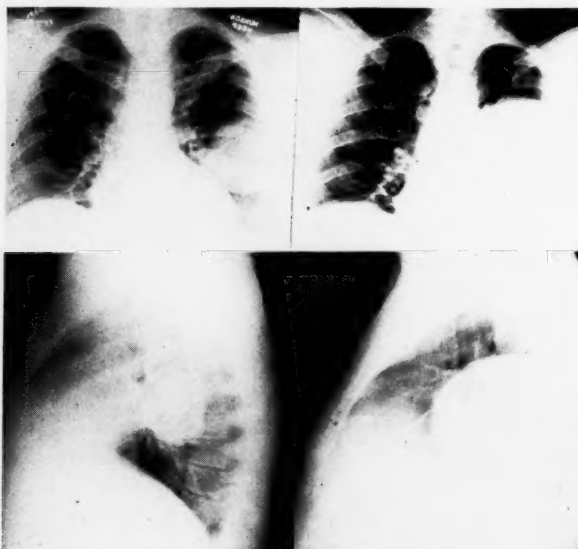


FIG. 3.—Primary intrapulmonary sarcoma. The roentgenograms showing the small tumor were made in November, 1939, and the larger tumor in December, 1940, five days before total pneumonectomy. The symptomless tumor was discovered in July, 1939, during a routine physical examination in another clinic, where the patient was advised to reduce his excessive weight (223 pounds at time of pneumonectomy) and to have another roentgenologic examination in from three to six months. As the November, 1939 (four months later) roentgenograms showed no growth, the patient was advised to have another roentgenologic check-up later (which he deferred for a year). In October, 1940, a "cold" was followed by persisting dyspnea, pain and cough, with whitish blood-streaked sputum. Bronchoscopic biopsy showed a submucosal sarcoma 2 cm. distal to the left upper lobe orifice. Thorough examinations revealed no extrathoracic primary neoplasm. Pathologic examination of the removed lung showed an intrapulmonary, encapsulated, soft, gelatinous, whitish, spindle cell sarcoma that had characteristics suggesting only local malignancy and an origin from a neurofibroma. Two lymph nodes, removed from the surface of the esophagus immediately below the inferior pulmonary vein, showed no evidence of metastasis. The patient was discharged from the hospital 46 days after operation, in excellent health except for a small residual empyema. Patient referred by Dr. E. F. Sladek, Traverse City, Michigan.

static lesions is obviously important. Even though no renal mass can be felt, a circular, circumscribed intrapulmonary tumor is sufficiently suggestive of a metastasis from an hypernephroma to justify pyelograms.

Malignant erosion of ribs, vertebrae, or sternum, in contradistinction to the thinning of bone by simple pressure, can be determined in some cases only from Potter-Bucky roentgenograms made in suitable projections. Thoracoscopy after the aspiration of pleural fluid and the substitution of air, may reveal the parietal pleural implantation of a malignant tumor that roentgenograms may have failed to disclose; otherwise, thoracoscopy almost never is capable of determining operability or of furnishing information of value that cannot be obtained by other means. As approximately 75 per cent of bronchial neoplasms are visible bronchoscopically, bronchoscopy is not only invaluable in determining the type of the lesion but, more importantly

from the surgical point of view, the exact position of the lesion in the tracheobronchial tree. Bronchoscopy may also furnish information of value in some cases in which the neoplasm has not arisen in the larger bronchi. Pneumoperitoneum is occasionally useful in distinguishing between supra-diaphragmatic and infradiaphragmatic neoplasms.

The following symptoms and signs are strongly suggestive of a malignant neoplasm and of inoperability: Dysphagia, paralysis of the recurrent laryngeal, or phrenic nerve, Horner's syndrome, hemorrhagic pleural fluid, serous pleural fluid in the presence of a small tumor, dilated veins, a sudden increase in the size of a tumor, severe pain, and rapid loss of weight. None of these symptoms or signs should, however, be accepted as absolute proof of either

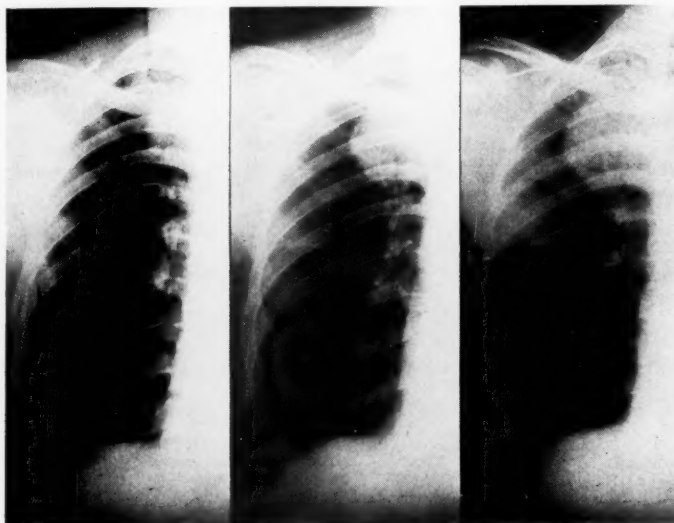


FIG. 4.—At the time of the left-hand roentgenogram (4-5-40) the patient, a male, age 47, was admitted to a well-known tuberculosis sanatorium because of fatigue and bloody, mucoid sputum, of one month's duration, but without pain, anemia or loss of weight. Tuberculosis was tentatively diagnosed. During the following four months, nine examinations of the sputum were negative for tubercle bacilli. A malignant neoplasm was promptly suspected, but operation was deferred because of two negative bronchoscopic examinations, and in spite of the progressive growth of the lesion as seen in the subsequent roentgenograms of 7-9-40 (middle) and 9-1-40 (right).

Total pneumonectomy, on 9-23-40, revealed medullary squamous cell carcinoma, Grade III, the bronchial origin of which in the right upper lobe bronchus was beyond bronchoscopic vision. Many mediastinal lymph nodes were removed which showed metastases. The patient died, 1-2-41, from cerebral metastases. There is a reasonable presumption that pneumonectomy at the time the first roentgenogram was taken would have cured the patient. Patient referred by Dr. Hillis Seay, Huntersville, N. C.

malignancy or inoperability as all of them have been observed in cases of benign neoplasm. Horner's syndrome may occur with a benign neurofibroma involving the sympathetic chain. The sudden increase in the size of a tumor, while strongly suggesting malignancy, may be due to hemorrhage within a degenerating benign neoplasm or to the rapid increase in the secretions of a cyst, perhaps from infection. Well circumscribed extrapulmonary neoplasms may be malignant, although most of them are benign. Most circumscribed intrapulmonary neoplasms, however, are malignant bronchogenic carcinomata (Fig. 4). While most neoplasms that are not well circumscribed are malig-

nant, such neoplasms may be benign, the loss of sharp definition at the edge of the tumor being due to inflammatory changes in the adjacent lung or pleura, or to localized collapse or atelectasis of the adjacent lung.

It is apparent from the statements in the last and other paragraphs that, apart from the diagnosis of malignancy from a biopsy of the tumor, or from a demonstrable metastasis, there are no reliable criteria from which the benign or malignant character of an intrathoracic neoplasm can safely be determined. The patient's safety, therefore, depends upon a prompt exploratory operation.

#### SURGICAL CONSIDERATIONS

Preoperative pneumothorax rarely adds information of value except in distinguishing between a pulmonary, as compared with a mediastinal or thoracic wall, origin of a tumor, which information does not alter the indication for operation. The statement has often been made that a preoperative pneumothorax is valuable in accustoming the patient to the conditions that will obtain at the time of operation in that pneumothorax stabilizes the mediastinum and, by shunting a large amount of blood into the lung of the opposite hemithorax, prepares that lung for additional work. I know of no evidence that supports this opinion, and there is good evidence that contradicts it. The wounding of the lung by the pneumothorax needle or the tearing of pleural adhesions and the lung by an increasing pneumothorax might cause a tension pneumothorax, a serous effusion, or an empyema, which might delay, complicate, or prevent the intended operation.

Immediately before operation, the internal saphenous vein at the ankle should be exposed for the introduction of a blunt needle, and 5 per cent glucose or normal saline solution administered, slowly at first. Since the routine administration of intravenous fluids during and after the removal of intrathoracic neoplasms was begun in my clinic, the condition of the patients has been definitely improved, and in a number of unusually difficult and shock-producing operations the continuous instillation of fluids, including blood, has probably been life-saving. The delay occasioned by the introduction of an intravenous needle *after* the actual necessity for fluids has become apparent may be responsible for fatal shock. The vein is exposed for the introduction of a blunt needle because this is more likely to function continuously than would a sharp needle introduced by puncture. An ankle vein is chosen because a needle in an arm vein might be disturbed by the operating team.

For anesthesia, I prefer intratracheal cyclopropane, perhaps with a small dose of avertin, in conjunction with procaine infiltration of the skin in the line of the intended incision, and of the intercostal nerves. Intratracheal anesthesia is valuable when administered by an expert anesthetist, but by no means indispensable. Should difficulty be encountered in the introduction of the tube, sufficient traumatic damage might be done to the throat and



larynx to interfere with easy respiration and expectoration after operation. Traumatic inflammation of the trachea would cause abundant tenacious secretions that might lead to serious complications. Furthermore, the larynx of a small child may not accept a tube with a sufficiently large attached aspirating catheter to permit the adequate aspiration of abundant tenacious secretions from the trachea, with the result that the patient might suffocate during the operation. From ten to 15 degrees of the Trendelenburg position of the operation table should be used in order to promote the drainage of pulmonary secretions toward the trachea and mouth, and in order to prevent the gravitation of mouth secretions to the lungs.

While certain neoplasms of the thoracic wall may properly be removed extrapleurally, virtually every intrathoracic neoplasm should be removed by a transpleural approach. The chief reason for this is that the wide exposure of the tumor that is obtained, in contradistinction to the relatively narrow exposure afforded in the course of an extrapleural operation, adds greatly to the patient's safety because of superior orientation of the mediastinal and other relationships of the tumor and because of the additional room given for the difficult operative manipulations. Furthermore, experience has shown that even a tedious, time-consuming attempt to keep from tearing the parietal pleura is usually unsuccessful. A tiny tear may allow a large amount of air to pass into the pleural cavity and build up dangerous pressure upon the lungs and mediastinum. If infection should occur in an extrapleural space, it would be transmitted to the general pleural cavity through a tiny tear in the parietal pleura. The traumatic serous effusion that forms as a result of the removal of an intrathoracic tumor and that usually requires one or more aspirations, may be removed more readily and safely from the bottom of the pleural cavity (where it collects when a transpleural approach has been used) than from the bed of the tumor (where most of it would collect if an extrapleural approach, without tearing of the pleura, has been used).

The exact site of the incision in the thoracic wall for the best exposure of a tumor is a matter of major importance. Many surgeons prefer an anterior incision for tumors that are in the anterior part of the chest. In spite of the apparent reasonableness of this choice and the fact that the skin incision may be concealed beneath a woman's breast, I greatly prefer a long posterolateral incision for almost all anterior intrathoracic tumors, for the following reasons: (1) The wider field of exposure affords better orientation and more room for the operative manipulations, especially in the mediastinum posterior to the tumor, and gives an almost equally good exposure anterior to the tumor. (2) The posterolateral approach gives splendid access to tumors in the dome of the thorax, whereas an anterior approach gives poor access because of the intervention of the clavicle and subclavian vessels crossing the first rib. In certain cases, however, in which a tumor is invading the anterior thoracic wall, an anterior incision is preferable to a posterior incision and, in rare cases, a sternum-splitting incision for a combined extra-

pleural-mediastinal and cervical operation is best. (3) The postoperative stability of a posterolateral incision is greater than that of an anterior incision.

When the posterolateral approach has been chosen, a study of cases illustrated in the literature shows that in a surprisingly large percentage of them the wrong rib has been resected for the best exposure of the particular tumor. As a result, one or more additional ribs have needed to be resected or divided in order to obtain adequate exposure of the tumor, thereby weakening the thoracic wall during the important postoperative period. In a con-

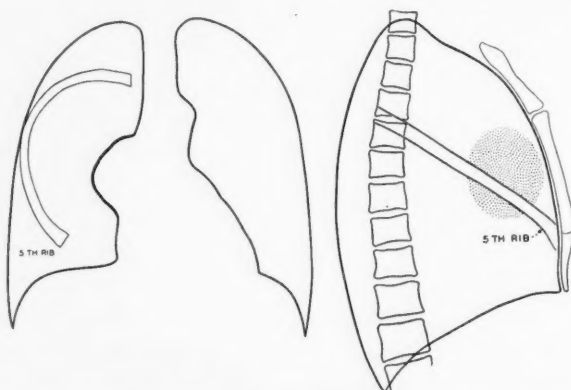


FIG. 5.—When access to an extrapulmonary tumor in the anterior two-thirds of the chest is gained through the resection of the posterolateral portion of a rib, the error is often made of resecting that rib whose posterior portion overlies the center of the tumor in the postero-anterior roentgenogram. In the case illustrated in the diagrams, this rib would be the eighth, which would be far too low. As the widest working space is approximately between the posterior and anterior axillary lines, the fifth rib should be removed for the best exposure of this tumor.

siderable number of reported cases, four or five ribs have been resected or divided for small or medium-sized tumors for which the resection of a single rib to the midaxillary or anterior axillary line should have been sufficient. In the case of tumors situated in the middle or anterior third of the chest, the common mistake is made of choosing for resection that rib whose posterior end overlies the center of the tumor in the postero-anterior roentgenogram; the removal of the posterolateral portion of this rib places the surgical working space far too low in relation to the tumor (Fig. 5).

For tumors that lie in contact with the posterior thoracic wall, a less extensive length of rib should be resected than for tumors in the anterior two-thirds of the chest; this rib should be the one that approximately overlies the upper third and lower two-thirds of the tumor in the postero-anterior roentgenogram. As most tumors lying snugly in the costovertebral gutter cannot be removed satisfactorily after the resection of only one rib, one or more adjacent ribs and intercostal bundles usually need to be divided posteriorly so that, when the ribs have been separated, a triangular opening, with its base posteriorly over the tumor, is formed. The removal of a 2-cm. length of a rib close to the tip of the vertebral transverse process and entirely

beneath the sacrospinalis muscle is preferable to the simple division of a rib because the resection of a 2-cm. portion prevents the postoperative pain that would occur from the rubbing of the divided ends against one another. Drilling and wiring the rib ends together as a part of the closure of the wound is entirely unnecessary if the 2-cm. portion that was resected lies entirely beneath the sacrospinalis and if the incision through the bed of the long length of rib that was resected is firmly closed.

The posterolateral resection of the seventh rib is usually used for a lower-lobe lobectomy, of the sixth rib if both the lower and middle (or lingular portion of the left upper) lobes are to be removed, and of the fifth rib if the entire lung is to be removed. Several surgeons, who have had much experience with total pneumonectomy, prefer the anterior approach, a perimammary incision, splitting of the pectoralis major over the third intercostal space and a parasternal incision of this muscle over the cartilages that are to be divided, a long third intercostal space incision and the division of the third, fourth, and perhaps also the second and fifth costal cartilages. I have used both approaches for total pneumonectomy and greatly prefer the posterolateral approach. Incidentally, lobectomy and pneumonectomy, as well as the removal of extrapulmonary neoplasms, whether by the posterolateral or anterior approach, may be carried out through an intercostal incision with or without the division of one or more ribs or cartilages, but without the resection of any rib. The incision through the thoracic wall is, however, facilitated by the resection of a rib, which later regenerates from the periosteum.

The rapid opening of the rib spreader often causes a reflex stoppage of respiration for a few moments. The spreader should be temporarily relaxed until normal breathing has reestablished itself, and then gradually reopened.

The preponderance of opinion among thoracic surgeons is that both intrapulmonary and extrapulmonary neoplasms should be removed in one stage when feasible.

If encapsulated extrapulmonary tumors are approached from within the pleural cavity, the parietal pleura and any subjacent "false capsule" tissue should be incised over the tumor and the dissection carried out in the extracapsular tissue plane. Since the chance of complete removal of a densely

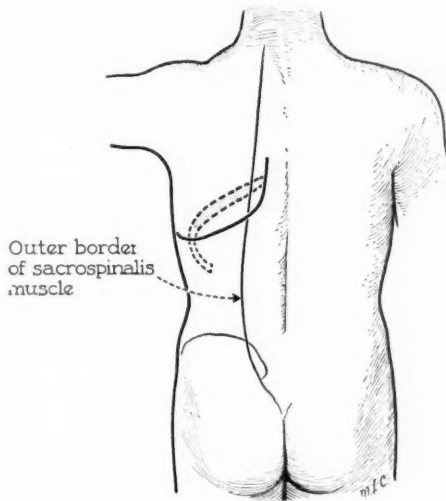


FIG. 6.—Imbrication of the incised layers of the thoracic wall. The vertical part of the incision in the skin and extracostal muscles is made over the sacrospinalis muscle, and the horizontal part below the portion of rib to be resected (shaded portion). Imbrication may prove useful in preventing the sucking of air into the pleural cavity, with resulting infection, should the incision heal imperfectly.

adherent cyst wall is enhanced when the dissection is carried out upon an intact cyst, every effort should be made not to rupture the cyst. Likewise, care should be taken not to tear the capsule that sometimes occurs around soft, friable, extrapulmonary malignant neoplasms since further operative manipulations in the presence of a tear of the capsule are likely to cause successive parts of the tumor to break away, with sharp accompanying hemorrhage that can be checked only by pressure.

A broad surface of the lung is often diffusely and rather firmly adherent to large extrapulmonary tumors. Separation can usually be effected by gentle finger dissection, with the occasional use of sharp division of tough adhesions that might cause more or less deep tears of the lung, if an attempt were made to rupture them with a finger. The profuse brief momentary hemorrhage that often occurs is best controlled by the temporary snug packing of the cleft between the lung and the tumor with dry gauze. Persisting bleeding points on the raw surface of the lung require ligation, and areas of injured alveoli and bronchioles from which air continues to leak should be oversewn with fine catgut. Heuer and Andrus recommend the resection of a "lappet of lung" that might be torn by the primary separation of its adhesions to the tumor. Such a resection would obviously be obligatory if the tumor were actually invading the pulmonary tissue.

Most extrapulmonary tumors receive their blood supply at scattered points on their circumference; rarely (except in the case of neurofibromata arising from an intercostal nerve or the sympathetic chain) can the surgeon discover a single well-defined pedicle. Numerous thick bands of tissue connecting the capsule and mediastinal or other tissues may, however, require ligation. Heuer and Andrus recommend the placing of a Shenstone lobectomy tourniquet around the site of origin of a tumor, especially one at the apex of the thorax, in case the tumor fills the operative field and thereby prevents the checking of hemorrhage and the guarding of important mediastinal structures under vision. It is apparent that the surgeon would need to satisfy himself that the tourniquet did not include any important mediastinal structure.

Since there is evidence to indicate that stimulation of the vagus or sympathetic nerve chain in the mediastinum may cause cardiac or respiratory stoppage, and since several actual cases of such stoppage have been reported as presumably due to the accidental operative stimulation of one or the other of these nerves, I recommend that they be directly injected with 1 per cent procaine solution through a fine needle, if the surgical situation requires that they be disturbed by dissection or if circumstances should require that they be divided. Obviously, the vagus nerve should be injected inferior to its recurrent laryngeal branch.

At intervals of from five to 15 minutes during intrathoracic operations, the lungs should be partly inflated by a moderate increase of the pressure in the gas anesthesia apparatus in order to overcome a tendency toward a

persisting atelectasis and impaired pulmonary circulation from prolonged pulmonary collapse. Such intermittent inflation is especially important when the lung on the side not being operated upon is partially collapsed by a great displacement of the mediastinum.

Patients requiring total pneumonectomy or lobectomy for carcinoma or other neoplastic lesion of the lung may have broad areas of exceptionally dense adhesions between the visceral and parietal pleurae that cannot be safely divided by the customary alternating blunt and sharp dissection. When such areas of dense adhesion represent an inflammatory reaction and not a neoplastic invasion of the thoracic wall, the simplest method for the separation of the lung from the thoracic wall is the incision of the parietal pleura around the area of dense adhesion, followed by the extrapleural separation of the lung and its overlying adherent pleurae from the costal periosteum and intercostal muscles by finger dissection. In such cases, the line of cleavage in the extrapleural tissues can often be readily developed. The leaving of a raw patch of thoracic wall, uncovered by parietal pleura, has no deleterious effect upon the patient's postoperative course. In principle, a somewhat similar maneuver may be used when a tumor is densely adherent to the costal periosteum; the periosteum may be incised just beyond the tumor and the densely adherent periosteum and tumor stripped away as a unit from the rib, which, then, is left bare on its inner surface.

An air-tight closure of the incision in the thoracic wall is important, especially with regard to the prevention of sucking of air into the pleural cavity, which would prove to be a serious postoperative complication (Fig. 6). Closure of the long incision in the parietal pleura and in the periosteal bed of the resected rib may be made with continuous or interrupted sutures placed close together, usually after relaxation of the incision with pericostal sutures around the two ribs adjacent to the pleural incision. Only rarely can the pleura and periosteum be sutured air-tight from the lateral edge of the sacrospinalis muscle to the posterior stump of the resected rib. This gap in the air-tight closure of the pleura can, however, be covered air-tight by suturing the lateral edge of the sacrospinalis muscle (which must, therefore, be carefully protected against being torn at the time it is separated from the ribs at the beginning of the operation) to the intercostal muscles and to one of the pericostal sutures.

The lung should not be inflated by the use of highly positive pressure in the intratracheal tube or face mask before closure of the incision because there is evidence that such inflation may rupture pulmonary alveoli. It is important, however, that the lung should be expanded as soon as possible after operation so that it will completely fill the pleural cavity. The reasons for this are: (1) That the removal of all the air from the pleural cavity prevents the driving out of this air by coughing into the layers of the thoracic wall; (2) the complete expansion of the lung brings the visceral and parietal pleurae in contact with one another; pleural adhesions then tend to form rapidly,



thereby preventing pleural infection or limiting it if it should occur; (3) complete expansion of the lung improves the cardiorespiratory functional reserve and, therefore, combats any tendency toward dyspnea, anoxemia and cardiocirculatory decompensation. Partial expansion of the lung may be obtained before the completion of the operation by leaving a catheter, attached to suction tubing, in the pleural cavity until just before the last suture that will produce an air-tight closure of the wound is to be tied. Shortly after operation, a bedside roentgenogram, made preferably in the sitting or semisitting position, should be obtained in order to determine if more than a little air remains in the pleural cavity. If it does, it should be removed by needle aspiration by means of "initial pneumothorax technic."

Space does not permit an adequate discussion of the conditions in which immediate tube drainage should be used after the removal of intrathoracic neoplasms. The indications for tube drainage are relatively rare, one of the most important being when any leakage of air from the lung (resulting from injury during the freeing of a tumor from the lung) persists at the time of closure of the thoracic-wall incision. Reliance upon intermittent needle aspiration of reaccumulating air might result in dangerous pressure upon the lung and mediastinum, and in progressive mediastinal and generalized body emphysema. The drainage tube should be removed early—as soon as the roentgenologic and physical findings indicate that leakage of air from the lung has ceased. Gross contamination of the pleural cavity from the spilling of the infectious contents of a tumor or from the opening of an infected lung may make immediate tube drainage advisable. There is, however, an increasing tendency not to drain such cases routinely but to rely upon a thorough lavage of the pleural cavity and the application of sulfanilamide or sulfathiazole crystals if contamination has occurred, and upon the rapid and complete expansion of the lung by needle aspiration of all pleural air immediately after closure of the thoracic wall incision, in order to bring the visceral and parietal pleurae in contact, thereby eliminating the dead space and fostering pleural adhesions that may wall-off pyogenic organisms before infection occurs.

The routine administration of oxygen during the first day or two after the removal of intrathoracic neoplasms is advisable. The patient should be directed to cough and expectorate any secretions that may be in the bronchi at frequent, regular intervals in order to prevent anoxemia, respiratory distress, or pulmonary infection from the accumulation of infectious secretions. Any air that may remain in the pleural cavity after the initial postoperative aspiration, as determined by bedside roentgenograms or physical signs, should be aspirated until virtually all the air has been removed. A variable amount of pleural fluid forms for several days after every operation involving either the inner or the outer surface of the pleura. This fluid should be aspirated daily, or every two or three days (depending upon the rapidity of its formation, its amount, and other circumstances) in order to prevent its causing an unnecessary load upon the heart, great vessels, and lung from pressure, and

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in order to remove a culture medium that might be used by any pyogenic organisms that had gained access to the pleural cavity.

### CONCLUSIONS

Dangerous delay in the diagnosis of intrathoracic neoplasms is frequently caused by their mode of onset, symptoms, physical signs, and roentgenographic appearance being strikingly similar to those of the more common thoracic diseases. In the interpretation of roentgenograms, a diagnosis of an interlobar effusion or other type of encapsulated effusion, simple atelectasis, tuberculosis, bronchiectasis, pulmonary abscess, pneumonia, or nonneoplastic enlargement of the hilar or mediastinal lymph nodes is frequently made when the lesion is actually a neoplasm.

The accurate preoperative pathologic diagnosis of intrathoracic neoplasms, apart from esophageal carcinoma and those bronchogenic carcinomata that can be biopsied endoscopically, is virtually impossible. In many instances, the surgeon cannot tell before operation whether the tumor is benign or malignant and, if it should be malignant, whether or not it is removable. As certain benign tumors are potentially malignant and as many malignant tumors may be removed completely, virtually every case of intrathoracic tumor should be promptly explored surgically if there is no evidence of metastasis or hopeless invasion of the adjacent thoracic walls, and if the patient's general condition permits.

Good results following the removal of intrathoracic neoplasms, both with regard to a low mortality rate and an uncomplicated convalescence, depend greatly upon the observance of certain special preoperative, operative and postoperative principles.

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DISCUSSION—DR. STUART W. HARRINGTON (Rochester, Minn.): I have been greatly interested in Doctor Alexander's excellent presentation of intrathoracic neoplasms and I am pleased that he has emphasized the difficulties that are often encountered in establishing a definite clinical diagnosis in these cases. He has emphasized the importance of instituting surgical treatment early, which I believe is of paramount importance in those cases in which surgery is considered, but I do not believe that surgical intervention should be instituted until a thorough investigation is carried out both clinically and roentgenologically. The most important lesions to be ruled out before surgery is instituted are lymphoblastomata and aneurysms. The clinical manifestations of these tumors are often meager and rarely pathognomonic, although they are always of great value when correlated with the roentgenologic findings in establishing a diagnosis and in determining the type of treatment to be instituted.

The roentgenologic examination plays a most important rôle not only in the recognition but also in the differential diagnosis of these lesions. Doctor Alexander has pointed out that all of these tumors are potentially malignant, and one of the important factors in their treatment is early surgical intervention before they have undergone malignant change. Such early removal is made possible chiefly because of the roentgenologic recognition of the tumors. As valuable as roentgenograms are in the diagnosis of these lesions, it is not always possible to make a definite diagnosis of the growth even when utilizing all of the roentgenologic methods now employed, and in many instances it is impossible to differentiate between benign and malignant lesions, which emphasizes the importance of surgical intervention without any appreciable time-interval of observation.

Doctor Harrington then demonstrated the value of the lateral roentgenograms in determining not only their importance in aiding in establishing a clinical diagnosis but also in their value in determining methods of approach. The most common tumors in the anterior mediastinum are the teratoid tumors, the most common tumors located in the posterior mediastinum are usually the neurofibromata, and the tumors located in the midportion of the thorax and which are often the most difficult to differentiate roentgenologically, are usually the lymphoblastomata and aneurysms.

DR. FRANK B. BERRY (New York, N. Y.): I should like to mention one additional method of differentiation between the aneurysms and the tumors, and that is in the use

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of diadrast intravenously according to the technic of Robbe and Steinberg, which we have found most helpful.

I should like to stress, as Doctor Alexander has, the early operation or exploration for these tumors, which sometimes, as we have found, has to be done over the protest of some of our medical colleagues, because it is certainly true that the smaller they are, the safer is the operation and the easier the removal.

We recently had an experience with a patient, a girl, age 12, who had a dermoid cyst of the mediastinum. While she was on the medical ward a fluid level suddenly appeared in the cyst indicating a rupture into the lung. Fortunately, the cyst did not become infected and removal was effected without any accident.

I should also like to put on record that we have had one case of a diaphragmatic hernia through the foramen of Morgagni, similar to that shown by Doctor Harrington in that it contained only omentum, and it was as much of a surprise to us as it apparently was to him.

DR. EDWARD D. CHURCHILL (Boston, Mass.): Doctor Alexander's very instructive series of cases was chosen, with great skill, to show the difficult decisions we face in the surgical treatment of intrathoracic neoplasms. He brought out one point that perhaps could be stressed a bit more, and that was that the early or the first symptoms caused by many of these tumors are interpreted as an ordinary unimportant complaint, usually pneumonitis or "pneumonia."

A few years ago, when the battle was raging between advocates of resection of the prostate by one method or another, someone said that Florida was full of elderly gentlemen wearing penile clips. I can say now, with the same exaggeration, that Florida is full of elderly gentlemen with cancer of the lung, who have been sent there for their cough. We see them wending their way back about this time of year, or we see them being referred back north by Florida physicians.

The point about roentgenotherapy is an important one. Only if very conclusive evidence exists that the tumor is of the lymphoblastoma series should a preliminary trial with roentgenotherapy be given. I am delighted to see that radiologists are more and more inclined to refuse to give treatment without a pathologic diagnosis.

Now about the question of operation. In general, I agree with Doctor Alexander that we must take a stand for a liberal policy of exploration in this type of case. Twenty years ago thoracic surgery was concerned with the mechanical physiology of the thorax—such problems as the difference between an open and a closed pneumothorax, pressure pneumothorax, mediastinal flutter, vital capacity, and differential pressure anesthesia.

During this period, even our distinguished president was alarmed about what he called the "Eclipse of Anatomy" by physiology, and gave an address before this association on this topic. The word eclipse, however, was wisely chosen, because no eclipse is ever permanent, and as soon as these questions were settled, the sun came out again. In the past ten years thoracic surgeons have been busy with the essential spade work in anatomy and pathology.

Now we are faced with some very difficult physiologic problems of a new type. Many of the patients concerning whom we are called upon to make a decision regarding operation present themselves with a very low margin of respiratory reserve from degenerative cardiorespiratory diseases.

We do not have to go back very far in the history of abdominal surgery to come to the time when technical advances applied solely on the basis of an anatomic-pathologic approach to surgery, resulted in catastrophies, particularly in the patients with low margins of safety. Many of these catastrophies can be avoided to-day, by attention to physiologic phenomena, such as alkalosis, acidosis, inorganic salt balance, water balance, and hemo-concentration.

The surgeon faced with the type of decision that Doctor Alexander has portrayed, in a patient with a low margin of safety in cardiorespiratory reserve, from age, emphysema, cardiac insufficiency, or chronic pulmonary infection, must, at times, compromise. Not infrequently, he must content himself with the argument: In the case of this particular man, his best chance lies in this not being a malignant tumor, rather than in my being able to do anything effectively about it, if it is.

If the scope of thoracic surgery is to be further extended we need now to conduct a more intensive study of the disturbances peculiar to the patient with a low margin of

safety in cardiorespiratory reserve. Many of the same problems that were faced in abdominal surgery will have to be reconsidered and modified for the physiologic functions peculiar to the thorax. Not only problems of adequate oxygenation but of  $\text{CO}_2$  excretion, and the effect of  $\text{CO}_2$  retention on the inorganic salt metabolism must be taken into account. Until these problems are solved we must, from time to time, be willing to maintain conservative limits both in the extent of operative procedures and even in the advocacy of exploratory thoracotomy.

DR. WILLIAM D. ANDRUS: (New York, N. Y.): Doctors Alexander, Harrington and Churchill have stressed the variation in the signs which may be associated with the neoplasms within the chest other than those of pulmonary origin. As has been pointed out, careful study and care of these patients, together with modern methods of anesthesia, make operation a relatively safe procedure.

The same criteria have come to hold in dealing with operations upon mediastinal and other intrathoracic neoplasms that apply elsewhere. Adequate exposure is of tremendous importance. It is very much less dangerous to make a much wider opening in the chest in order to be able adequately to deal with the surroundings of a neoplasm than to be crowded for space.

Doctor Alexander has stressed the fact that none of the criteria which have sometimes been held to be characteristic of malignancy are absolutely accurate. The location of the tumor is highly suggestive in many instances, as for example, the anterior and anterior-superior mediastinum in dermoid cysts. However, the location of the tumor is no more accurate in determining the exact diagnosis or its benignancy or malignancy than is the location of the gastric ulcer in determining its possible malignancy. Size is no criterion, for some of the largest tumors may be benign.

I should like to stress the characteristic of one group of tumors which have seemed to us to be of considerable importance, namely, those that have reached a very considerable size without producing pressure symptoms on the mediastinum. Those tumors, while they may be embryonal and, therefore, possibly malignant in character, are in essence benign. I am referring to the so-called fibrolipomata or fibrolipomatous myxomata. We have recently had two cases of this type, one of which weighed 1,800 Gm. and yet caused no symptoms. It was picked up casually on roentgenologic examination following, as in many instances occurs, a respiratory attack which seemed to call attention to the tumor.

Another tumor, in a patient weighing about 92 pounds, proved to be a fibrolipomyxoma of a questionable malignancy, and weighed nearly 4,000 Gm.; in other words, close to 10 per cent of the patient's weight. This tumor was successfully removed, and the patient has made a satisfactory recovery.

In dealing with these tumors, it can be said that the tumors that can be removed are either benign, or the fact that they are malignant comes somewhat as a surprise after the pathologist has examined them. Every effort should be made to remove these tumors completely, and this is particularly true of the dermoids, where the mortality is very much the lowest, and the cures very much the highest when the tumor is completely removed.



## TOTAL THORACIC AND PARTIAL TO TOTAL LUMBAR SYMPATHECTOMY AND CELIAC GANGLIONECTOMY IN THE TREATMENT OF HYPERTENSION\*

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RECENT SURGICAL TREATMENT of hypertension has been directed, primarily, toward a sympathetic denervation of the splanchnic area. Several approaches have been employed. Ventral rhizotomy consisting of intraspinal section of the lower six thoracic and first two lumbar anterior spinal nerve roots has been employed in a limited number of patients. Adson, Craig, and Brown<sup>1</sup> report 27 patients, and Heuer<sup>2</sup> 21 patients treated and studied by him and Page. Both reports show a limited incidence of serious surgical complications, and the procedure appears to have been abandoned. Subdiaphragmatic resection of the splanchnic nerves and part of the celiac ganglia together with resection of the first and second lumbar ganglia has been employed by Adson. Allen and Adson reported its use in a series of over 300 cases, without an operative death. Blood pressure reduction is given as good or fair in 31 per cent, and temporary or poor in 69 per cent of their patients. Supradiaphragmatic extrapleural splanchnicectomy consisting of resection of a long section of the greater splanchnic nerves above the diaphragm together with the tenth, eleventh, and twelfth thoracic ganglia, the intervening sympathetic chain, and the lesser splanchnic nerves, has been employed by Peet in more than 700 patients. Studies of 350 of these patients have been reported by Peet, Woods, and Braden.<sup>4</sup> There was a 51.4 per cent significant reduction in blood pressure. They have operated upon many patients with advanced hypertension. Their operative mortality is given as 3.4 per cent.

Celiac ganglionectomy and denervation of the peri-aortic complex of sympathetic nerves and ganglia has been carried out by Crile<sup>5</sup> in 213 patients. Transdiaphragmatic removal of the lower four thoracic and first, or first and second lumbar sympathetic trunk ganglia together with a long segment of the splanchnic nerve has been performed by Smithwick<sup>6</sup> in a large series of patients. Emphasis is placed upon the importance of the postoperative postural hypotension achieved.

A review of these reports and of reports of smaller series of similar operations performed by other surgeons gives the impression that although worthwhile improvements have been obtained in some patients, the therapeutic results, as a whole, have left much to be desired. Clinical and symptomatic benefit have been reported much more frequently than blood pressure lowering. A proper evaluation of the effect of any form of therapy in hypertension is always difficult because of the variety of the symptoms encountered and the

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difficulty of establishing a definite control. The value of splanchnic area denervation in hypertension has been extensively debated.

The rôle of the sympathetic nervous system in experimental neurogenic and renal types of hypertension has been reviewed in a previous report.<sup>7</sup> It has been demonstrated that splanchnic area denervation does not appreciably alter a normal dog's blood pressure, or the hypertensive response to increased intracranial pressure, or the level of the chronic neurogenic hypertension that follows division of the buffer or depressor nerves from the carotid sinuses, heart, and aortic arch. Complete paravertebral sympathectomy in dogs, employing a modification of the technic originally developed by Cannon and his associates<sup>8</sup> has been demonstrated to lower temporarily a normal dog's blood pressure, to eliminate the hypertension response to increased intracranial pressure, and to lower the blood pressure of neurogenic hypertensive dogs for a time to the vicinity of the normal. These and other experiments suggested that total paravertebral sympathectomy might accomplish more in clinical hypertension than splanchnic area denervation alone, especially if there should be an element of a neurogenic nature in clinical hypertension. The recovery of some degree of central vasomotor control following total sympathectomy in dogs, as previously reported<sup>9</sup> is incomplete. It does suggest, however, that the vascular alterations achieved by the operation in clinical hypertension might be limited in duration.

Studies related to experimental renal hypertension of the type developed by Goldblatt and his associates<sup>10</sup> have offered little encouragement to sympathetic surgery in clinical hypertension. This renal type of hypertension persists in the experimental animal after total paravertebral sympathectomy.<sup>11, 12, 13, 14</sup> This observation demonstrates that the vascular bed is under an influence, probably humoral, the action of which is independent of the sympathetic nervous system. If clinical hypertension were primarily renal in nature, the large splanchnic vascular area denervated by operation would also be under the same humoral vasoconstrictor influence.

The possibility of improving the blood supply of the kidney and thus altering the formation of a renal pressor substance has been suggested by Peet.<sup>4</sup> Clinical studies of renal hemodynamics have, however, failed to show any consistent alteration following splanchnic area denervation in hypertensive patients (Foa, Woods, and Peet,<sup>15</sup> and Corcoran, personal communication).

The mechanism of hypertension in man is probably complex. It is generally accepted that it is mediated by an increase of the peripheral resistance offered by the vascular bed to blood flow. The extent to which processes comparable to experimental renal or experimental neurogenic hypertension may play a rôle in man in increasing the peripheral resistance has not been clearly demonstrated. Grollman, Williams, and Harrison,<sup>16</sup> Page, Helmer, Kohlstaedt, Fouts, Kempf and Corcoran,<sup>17</sup> and others, are developing tissue extracts which they report to be effective in lowering the blood pressure of renal hypertensive dogs and hypertensive patients. If these substances should prove to have specific action against the renal humoral mechanism, their use

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in patients would contribute a great deal toward an understanding of the etiology and, possibly, also toward the control of clinical hypertension. Until their availability and ultimate utility are demonstrated, surgical efforts in the treatment of hypertension appear to be justified.

Total paravertebral sympathectomy might accomplish more than splanchnic area denervation in the treatment of hypertension in man especially if, as is stated above, there should be a component of a neurogenic nature in clinical hypertension. A technic has, therefore, been developed for total paravertebral sympathectomy. This procedure has been attempted on 11 patients with varying degrees of success.

*Technic.*—The operation, when carried to completion, is undertaken in three stages, two thoracic and one abdominal. At each thoracic operation, the stellate ganglion and the entire thoracic sympathetic ganglionated chain, the entire length of the splanchnic nerve and its minor branches, and the major portion of the celiac ganglion of that side is removed. An effort is also made, but without marked success, to obtain through the diaphragm the first or first and second lumbar ganglia. Figure 1 shows the sympathetic anatomy involved. The third stage, in those instances in which it is employed, consists of a bilateral excision of the remaining portions of the lumbar sympathetic chains down to or including the fifth lumbar ganglion. The operation is of necessity transthoracic and transabdominal. The thoracic stages were performed under ethylene anesthesia, using positive pressure through a face mask, and the abdominal operation under either spinal or ethylene-ether anesthesia. Long alligator forceps, dissectors, hooks and scissors both straight and curved have been devised for dissection of the nerve roots and branches. A special oval-headed, malleable retractor is used for the lungs and a heavy malleable roundheaded retractor with two small hooks at the end for retraction of the diaphragm (Fig. 2).

Figure 3 illustrates the location of the incisions. The first incision is made in the axillary region over the third rib which is exposed and resected to the extent of about 12 cm. The thoracic cavity is entered through the rib bed. The lung is retracted, the sympathetic ganglionated trunk is located, and the pleura overlying its upper five segments is divided. Figure 4 represents the exposure



FIG. 1.—The relationships of the stellate ganglion, thoracic sympathetic chain, splanchnic nerves, celiac ganglion, and first portion of the lumbar sympathetic trunk. The proximity of the celiac ganglion and the diaphragm is illustrated.

of the upper sympathetic chain and stellate ganglion. The connections of the upper thoracic chain and stellate ganglia are severed. The incision in the pleura is then extended over the sympathetic chain to the level of the eighth thoracic ganglia exposing the beginning of the splanchnic nerve. Figure 5 represents this portion of the exposure. The roots of the ganglionated trunk

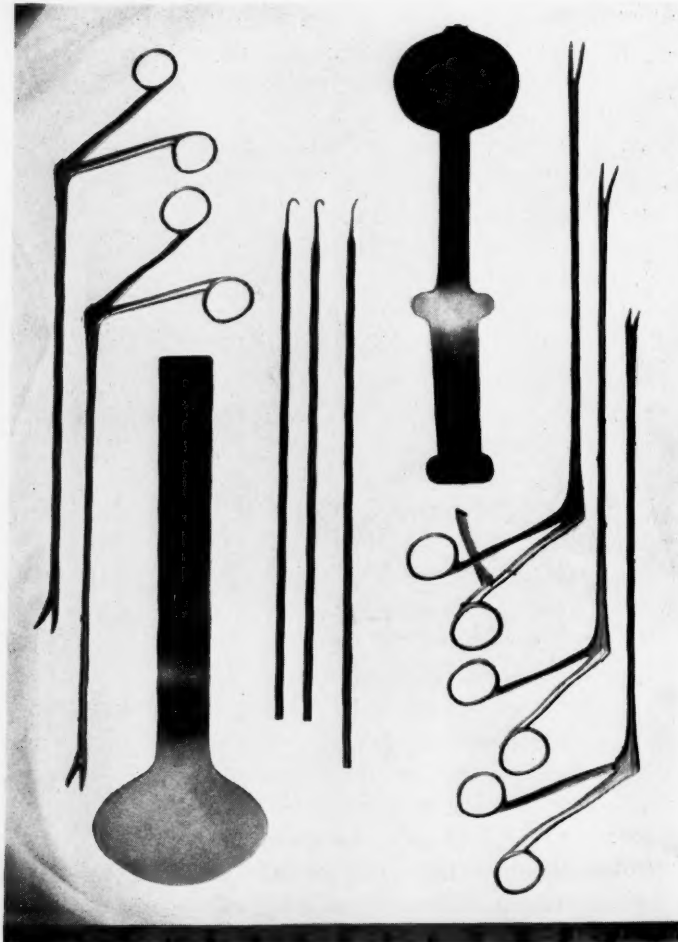


FIG. 2.—The special long alligator forceps; curved and straight scissors; dissector and hooks; oval-headed malleable lung retractor; and round-headed hooked diaphragm retractor used in the thoracic sympathectomy. The dissector is 12 inches in length.

are cut down to the eighth ganglion, the origin of the splanchnic nerve is freed, and the chain is dropped down into the lower thoracic cavity. The incision in the chest wall is closed.

A second lateral incision is then made over the course of the tenth rib and 12 to 14 cm. of its length is resected. The thoracic cavity is entered through the rib bed. The free end of the sympathetic chain is picked up and its remaining portion and the splanchnic nerve and its connections are dissected

# SYMPATHECTOMY FOR HYPERTENSION

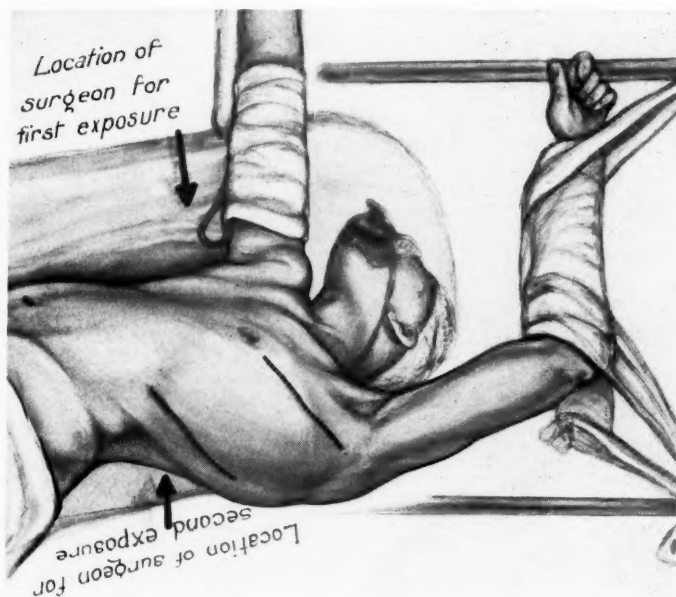


FIG. 3.—The position of the patient during the thoracic operation and the location of the two incisions used. The stellate and upper 8 sympathetic ganglia are dissected free through the upper incision and the remainder of the thoracic trunk, the splanchnic nerve, the celiac ganglion and, at times, the first or first and second lumbar ganglia are removed through the lower incision.

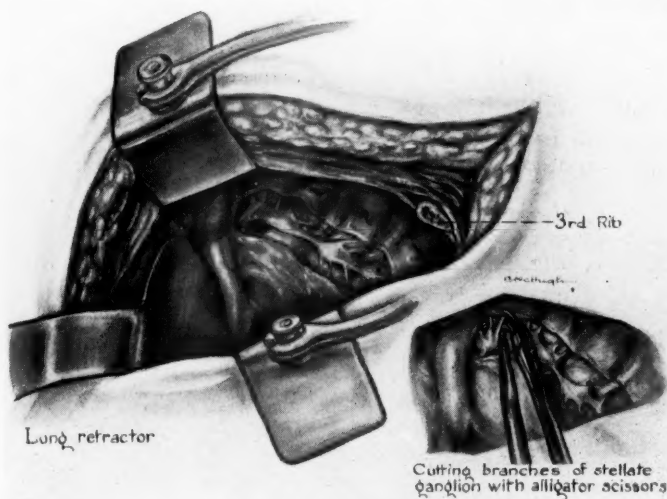


FIG. 4.—The stellate ganglion and the upper thoracic sympathetic trunk exposed through the incision in the bed of the third rib. The overlying pleura has been divided.



free down to the diaphragm. The pleura over the arch of the crux of the diaphragm is divided and the curved tip of the special round diaphragmatic retractor is placed in the arch. Strong retraction on this instrument partly inverts the diaphragm and allows the celiac ganglion to be pulled up through the diaphragm by traction on the splanchnic nerve after blunt separation of the adjacent diaphragmatic muscle. This ganglion is removed as completely

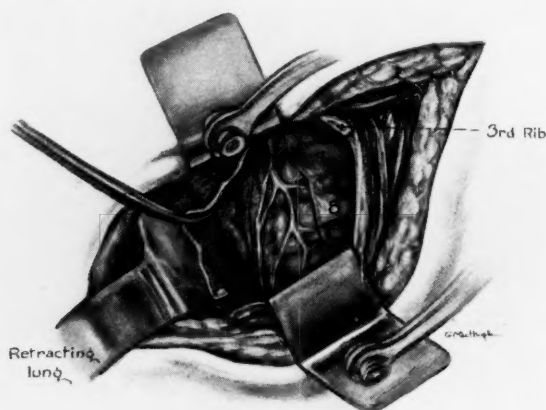


FIG. 5.—The origin of the splanchnic nerve at the lower end of the operative field, exposed by the incision through the third rib bed. The ganglionated sympathetic nerve trunk is freed through this incision down to D7 or D8.

as possible by dividing its distal connections. The sympathetic chain is then followed down through the crux of the diaphragm as far as possible and divided. Success in obtaining ganglia lower than the twelfth thoracic has been variable. Figure 6 represents this portion of the exposure. The thoracic portions of the sympathetic trunk, the splanchnic nerve and the celiac ganglion, and occasionally, also, the first or the first and second lumbar ganglia are thus removed. A medium-sized Pezzar catheter is then inserted into the pleural cavity through a stab wound between the seventh and eighth ribs in the mid-axillary line and the incision is closed. Air is evacuated from the thoracic cavity through the catheter and a negative pressure maintained for four or five days. Figure 7 illustrates a photograph of the specimens removed from the chest of one patient.

Of the 11 patients, eight had the thoracic procedures. One of these died after the first stage and one after the second. Three patients had both the thoracic and abdominal procedures. Brief case reports are presented.

#### ABBREVIATED CASE REPORTS

##### BILATERAL THORACIC OPERATIONS

**Case 1.**—J. W., female, single, age 18 at the time of operation. She had been observed to have a blood pressure of 176/124 three and one-half years earlier when seen in the Urology Clinic because of nocturia. Double ureter and kidney pelvis on the

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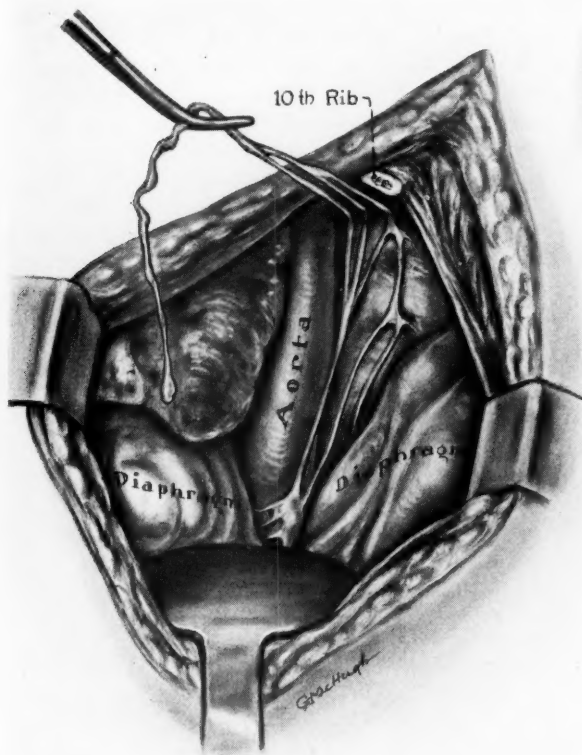


FIG. 6.—The exposure of the lower end of the thoracic sympathetic trunk and of the splanchnic nerves. The celiac ganglion has been pulled up through the diaphragm. It is removed, as are also as many of the lumbar ganglia as can be reached.

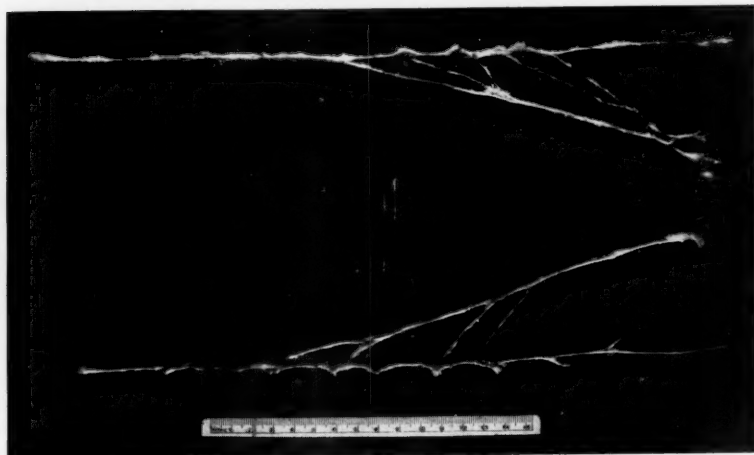


FIG. 7.—A photograph of the operative specimens removed from Case 10 during the bilateral thoracic operations. The stellate ganglia; splanchnic nerves; celiac ganglia; and, on one side, the first lumbar ganglion are shown.

right was observed. The patient had occasional periods of mild urinary infection and of albuminuria. The blood pressure rose gradually in spite of medical management and restricted activity until it ranged around 200/138. The patient complained of occasional severe headaches. Eyeground examination revealed generalized attenuation of the retinal arteries. There was a bilateral moderate exophthalmos. Rest and 0.6 Gm. of sodium amytal reduced the blood pressure from around 212/146 to around 170/120. The two stages of the bilateral thoracic paravertebral sympathectomy were carried out, with an interval of two weeks. The blood pressure between the two operations was as high or higher than before. After the second operation it fell, and three weeks later, at the time of discharge, ranged around 146/98 when the patient was supine. She has been observed seven months and two weeks following the procedure, and her last blood pressures are around 140/90 when supine and 104/70 when standing. Dizziness on standing was noticed during the first month after operation. The patient is now active with no complaints.

**Case 2.**—R. B., female, married, age 25 at the time of operation. She gave a history of nephritis, with blood and albumen in the urine between the ages of four and five. Three and one-half years before operation she developed headaches. Three years before operation she became pregnant and a blood pressure ranging around 180/110 was observed together with albumen and blood in the urine. A therapeutic abortion and sterilization were performed. Six months later the headaches became more severe and a blood pressure of 220/120 was recorded. Under medical management during the next two and one-half years, her blood pressure was observed to range around 180/110. In the hospital during the week before operation, it averaged 168/104. During this period of three years, there was no significant finding in the urine. With rest and 0.6 Gm. of sodium amytal her blood pressure dropped from 180/108 to around 140/90. The cold pressor test showed an elevation of 35 Mm.Hg. systolic and 30 Mm. diastolic. Eyeground examination revealed increased tortuosity of the retinal arteries. After the first stage, there was no change in blood pressure but after the second, there was a lowering to around 106/64 during a six weeks' postoperative period of observation. She has now been observed 14 months, during which her blood pressure has ranged around 120/70 supine and 100/64 standing. The patient is active with no complaints.

**Case 3.**—C. D., female, married, age 33 at the time of operation. Eleven and one-half years earlier, during a premature delivery, her systolic blood pressure was recorded at 220 Mm.Hg. After delivery, her systolic blood pressure varied from 180 to 220. One year and seven months before operation, she went through an episode of precordial pain, dyspnea, and swollen ankles. Six months before operation, she had a cerebral accident involving the right arm and leg and leaving extensive residual paralysis. Her blood pressure on admission was 242/148. During two weeks in the hospital, before operation it ranged between 286/170 and 200/120. The elevation with the cold pressor test was 20 Mm.Hg. systolic and diastolic. With rest and 0.6 Gm. of sodium amytal the pressure fell from 260/160 to 220/145. Papilledema, hemorrhage, exudation, and other advanced eyeground changes were present. Following the first thoracic operation, there was no reduction in blood pressure. Immediately following the second thoracic operation, the blood pressure ranged around 140/80. The patient, however, did not regain consciousness and 30 hours later developed respiratory failure. Artificial respiration was continued for several hours after which time circulatory failure developed, with death. Autopsy revealed a cavity in the left side of the brain 2.5 x 1.5 x 6.5 cm. in length running from the central white matter of the frontal lobe posteriorly to the caudal extremity of the lenticular nucleus. There was generalized cerebral arteriosclerosis with old and recent foci of encephalomalacia and old and recent perivascular hemorrhages in the pons. It is of interest that during the 30-hour postoperative period of reduced blood pressure, the patient excreted 1,600 cc. of urine.

**Case 4.**—I. M., married, female, age 38 at the time of operation, and had only one preoperative complaint, that of blurring vision requiring frequent changes in her glasses.

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Six months before operation her blood pressure was 220/120. Between then and the date of operation, it ranged around 210/118. In the hospital, the week before operation it averaged 180/114. Eyeground examination revealed only generalized attenuation of the retinal arteries. Rest and sodium amytal lowered the blood pressure from around 180/110 to around 135/90. The cold pressor test elevated the systolic pressure 35 Mm.Hg. and the diastolic 25 Mm. The two-stage thoracic procedure was carried out. During the 17-day interval between operations, no lowering of blood pressure was observed. It ranged around 150/102 during the four weeks in the hospital after operation. This patient developed a mixed psychoneurosis with secondary depressions. She fixed on the operation as the cause of all of her troubles. Hospitalization was carried out one and one-half, two, and four and one-half months postoperatively because of this psychiatric difficulty. Her blood pressure during these hospitalizations averaged 166/96, 144/96, and 150/100, respectively. She has since been more antagonistic, and one reading, seven and one-half months after operation, was 198/128 lying and 184/104 standing. The last blood pressure readings, 12 months after operation, were 144/102 lying and 112/84 standing.

**Case 5.**—E. R., a poorly nourished male, age 40 at the time of operation. He had consulted a physician four and one-half years earlier because of lack of appetite, dizzy spells, and headaches. His blood pressure then varied between 170/130 and 145/90. It gradually rose, and during the three and one-half years before operation ranged from 206/130 to 176/116. Fatigue, headaches, and dizziness persisted. One year before operation, he had a mild cerebral accident following which he could no longer perform his duties as a lathe operator. During the week before operation, his blood pressure averaged 178/116. Rest and 0.6 Gm. of sodium amytal lowered his blood pressure from 194/120 to around 165/105. The cold pressor test elevated it 24 Mm.Hg. systolic and 10 Mm. diastolic. Examination of the eye revealed irregularity and marked narrowing of the retinal vessels and some arteriovenous nicking. The two stages of the thoracic operation were performed 13 days apart, with no blood pressure lowering between. Sixteen days later the patient was discharged. The postoperative hospital blood pressure readings averaged 126/86. During eight months of postoperative observation the blood pressure ranged around 140/100 supine and 96/74 standing. He has occasionally had mild headaches but the fatigue and poor appetite persist and he considers himself unable to work.

**Case 6.**—H. S., male, age 42 at the time of operation. A year and one-half earlier headaches developed and eight months ago his blood pressure was 190 systolic. Six months before operation a cerebral accident occurred involving the right arm, leg, and face and making speech difficult. The blood pressure was 255/145. A month later recovery of the use of the leg began and he was able to walk. There was limited use of his arm at the time he entered the hospital. His blood pressure in the hospital before operation averaged 196/128. Sodium amytal lowered it from around 230/134 to around 160/120. The cold pressor test elevation was 70 Mm.Hg. systolic and 60 Mm. diastolic. Eyeground changes consisted chiefly of constriction of the retinal arteries with tortuosity of the smaller vessels. The patient received the thoracic operations with an interval of 14 days, during which there was no change of blood pressure. He then remained in the hospital six weeks during which time his blood pressure ranged around 146/90. He has been followed postoperatively for eight and one-half months and during that time has had a blood pressure ranging around 150/94 lying and 124/84 standing. He has now no complaints and is active although unemployed.

**Case 7.**—R. E., male, age 48 when operated upon. Four years before his blood pressure was reported to have been around 210/135. His complaints were chiefly fatigue, dyspnea after climbing one flight of stairs, and disturbance of vision. Eleven months before operation, hemorrhage and exudation were noted in the eyegrounds. Six weeks before operation his blood pressure was as high as 272/172. Papilledema, with marked progression of the hemorrhages and exudates, were noted. In the hospital before operation, the blood pressure ranged around 235/158. Rest and 0.6 Gm. of

sodium amytal lowered it from around 210/140 to around 185/120. The cold pressor test gave an elevation of 50 Mm.Hg. systolic and 45 Mm. diastolic. Right thoracic sympathectomy was performed. There was, as in the other patients, no lowering of blood pressure following this procedure. Sixteen days later a roentgenogram of the chest revealed the lungs to be clear; and the patient was sitting up out of bed. The second-stage operation was under consideration when he developed pneumonia followed by uremia, and, 21 days later, by death.

**Case 8.**—L. F. M., male, age 50 at the time of operation. Four years earlier he developed severe headaches and noticed occasional dizzy spells. During the last two years, these symptoms became more severe and the systolic blood pressure was over 200. Four months before operation, a cerebral accident occurred with a paralysis of the left arm and leg from which there has since been extensive recovery. The blood pressure was 252/140. During the week in the hospital before operation, it averaged 218/130. Rest and 0.6 Gm. of sodium amytal reduced the blood pressure from 228/120 to around 188/100, with two single readings of 166/88 and 150/90. The cold pressor test produced an elevation of 50 Mm.Hg. systolic and 30 Mm. diastolic. Eyeground examination revealed a thickened, slightly blurred nasal nerve fiber layer on the right disk and nicking, hemorrhage and exudation in the retina. Urea clearance determinations were at the lower limits of normal. Following the right thoracic sympathectomy, cardiac decompensation and pulmonary edema developed. These complications cleared up in about two weeks. No blood pressure lowering was observed in the 25-day interval that preceded the second stage. Cardiac and pulmonary complications were also observed after the second stage. During the next five weeks in the hospital, his blood pressure ranged around 156/90 supine. Seven months after operation, he was admitted to the hospital for two weeks during which time his blood pressure readings averaged 160/90. His readings in the out-patient department have been higher, ranging around 172/100 supine and 134/104 standing 12 months postoperatively. This patient while having less energy than formerly has no special complaints and is active.

#### BILATERAL THORACIC AND ABDOMINAL OPERATIONS

**Case 9.**—A. W., female, married, age 33 at the time of operation. Five and one-half years earlier she developed albuminuria and a systolic blood pressure of 290 in the fourth month of pregnancy. A therapeutic abortion was performed. During the next two years, the patient had several attacks of precordial pain. The blood pressure elevation continued. Dyspnea, palpitation, and ankle swelling had gradually progressed. She was first seen here at that time, and the blood pressure was 240/144. Eyeground examination showed the disks to be pale with hazy margins and tortuous capillaries on their surfaces. Arteriovenous compression, small hemorrhages, and exudates were observed in the retinae. Rest and 0.6 Gm. of sodium amytal lowered her blood pressure from 230/128 to 204/118. Cold pressor tests produced an elevation of 20 Mm.Hg. systolic and 30 Mm. diastolic. Thiocyanate therapy was employed for four months, with the blood pressure unchanged, averaging around 230/130. A bilateral supradiaphragmatic splanchnic area denervation, as advocated by Peet,<sup>4</sup> was then carried out by Dr. William Adams. The blood pressure averaged 190/122 for one week and then returned to its previous level. Three months later, thiocyanate therapy was again employed without appreciable effect. Fifteen months later, an attempt was made to complete the sympathectomy using the technic described above. All three stages were employed at one-month intervals. Following each stage, there was some lowering of pressure until after the abdominal operation it averaged for two weeks 174/108. It then gradually rose until at two months it reached an average supine of 220/130. She has been observed 11 months. The last blood pressure reading is 254/154 supine and 192/120 standing. The patient is moderately active with only occasional mild headaches. Swelling of the ankles is again evident.



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**Case 10.**—L. M., widow, age 40 at the time of operation, and had had headaches for about four years. She suffers from a severe anxiety neurosis that has persisted up to the present time, with only slight improvement. The first blood pressure readings a year and eight months before operation were 248/128 and 280/130. She was hospitalized four weeks at that time, and the blood pressure readings averaged 236/128. Thiocyanate therapy was without evident effect. The blood pressure continued for a year and six months around 250/134 with one high reading of 310/144. During four weeks of hospitalization preceding operation, there was some improvement in the mental state and the average blood pressure was 204/110. Eyeground examination revealed minimal hemorrhage and exudate and marked nicking but no papilledema. Rest and 0.6 Gm. of sodium amytal lowered the blood pressure from around 240/120 to around 160/90. The cold pressor elevation was around 35 Mm.Hg. systolic and 20 Mm. diastolic. The blood pressure during the 12-day interval between the thoracic stages was unchanged. Following the second stage it ranged around 180/96 for two months. The abdominal sympathectomy was then performed. The blood pressure during the next three weeks ranged about the same level. Four months later a single reading was 280/154. The patient was readmitted to the hospital for a week and the blood pressure averaged 192/108. Her latest blood pressure readings, 10 months after the third stage, range around 224/124 supine and 160/90 standing. She is active, and states that she feels better.

**Case 11.**—McK. T., male, age 44 at the time of operation. The blood pressure is known to have been elevated for seven years, starting around 180/110 and gradually increasing to around 210/130. The complaints were occasional headaches and attacks of numbness usually unilateral, involving the arms and legs. Eyeground examination revealed early edema of the disks with marked perivascular sheathing of the retinal vessels. Rest and 0.6 Gm. of sodium amytal lowered his pressure from around 200/112 to around 158/90. The cold pressor response was 40 Mm.Hg. systolic and 70 Mm. diastolic. Because of the possibility of an adrenal tumor, the abdominal sympathectomy including division of most of the splanchnic nerves was performed first. Exploration of the adrenal glands and kidneys revealed no gross pathology. Following this, the blood pressure ranged around 158/108 for 20 days, at which time the right thoracic sympathectomy was performed. In the 23 days that preceded the left thoracic sympathectomy, the blood pressure was around 150/102. Following this, it ranged around 128/80 for eight weeks. All of these readings were taken with the patient supine. The patient had a marked postural hypotension, with extreme dizziness, and it was six weeks after the last operation before he could walk about and be discharged. It is too early to evaluate the symptomatic change. Six months after operation his blood pressure readings were 140/100 supine and 76/54 standing.

**SUMMARY.**—A three-stage technic for removal of the thoracic and lumbar paravertebral sympathetic chains including the stellate ganglia, splanchnic nerves, and the major portion of the celiac ganglia has been described. This operative procedure has been employed upon 11 hypertensive patients. Three had only slight organic hypertensive changes, four had had cerebral accidents, three were old, severe long-standing hypertension, and one was a rapidly progressing severe hypertension with renal deficiency. Two of these patients, one with marked brain damage, and one with marked renal damage, died. The bilateral thoracic procedure only was employed in six patients and the three-stage procedure including the lumbar sympathectomy was employed in the remaining three. A complete loss of sweating has not been achieved. The iodine, starch, heat-sweating test has shown occasional patchy areas of sweating

in the apparently denervated areas in each patient. Figure 8 shows the dark areas of sweating in Case 11 after the three-stage procedure, and in Case 6 after the two-stage thoracic procedure.

This extensive sympathectomy has been demonstrated to be compatible with a relatively normal existence. The patients dress more warmly in cold weather and notice excess perspiration during warm weather in those areas still capable of sweating. Dizziness associated with postural hypotension has

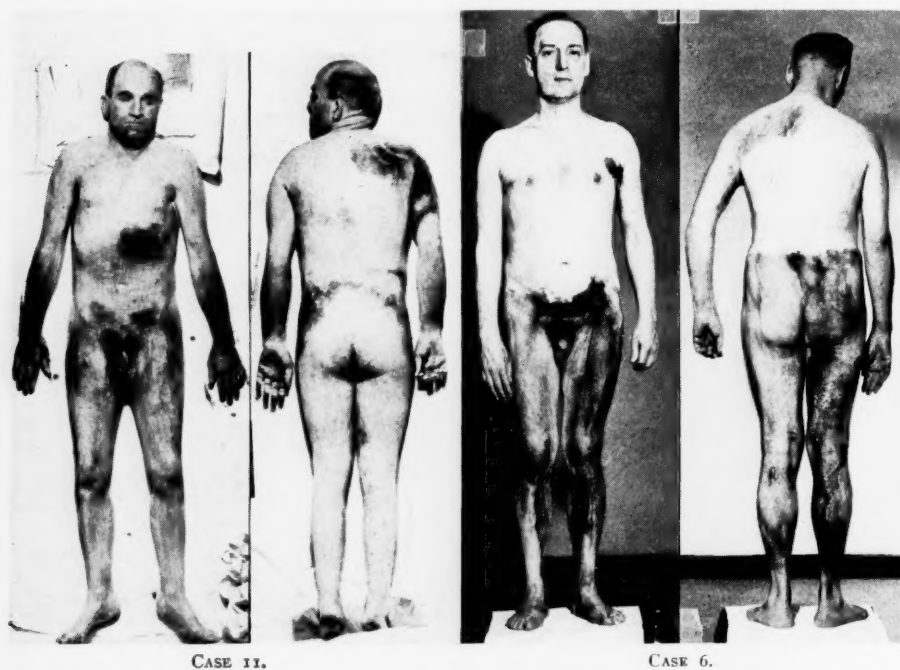


FIG. 8.—The dark areas of sweating visualized by the iodine, starch, and heat test in Case 11, after the three-stage sympathectomy; and, in Case 6, after the bilateral thoracic procedure. Areas of sweating are present in the regions supplied by the sympathetic trunks that have apparently been removed.

been troublesome only during the first few months. The bilateral Horner's syndrome has been distressing to only one patient, Case 4. A transient hyperactivity of the bowel has been noticed after each thoracic procedure in many of the patients. The pulse rate has been somewhat decreased. The response to stimuli such as the cold pressor test has been either unchanged or slightly diminished. The blood pressure lowering response to rest and sedation as in the sodium amytal test has been in most instances almost entirely abolished (Chart 1).

Some lowering of blood pressure has been observed on each patient. The lowerings of the blood pressure with the patient supine have varied from a transient one followed by a restoration to about the previous hypertensive level in Case 9, to a lowering to relatively normal values over a period of 14 months of observation in Case 2. The lowering of blood pressure with the

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patient standing, sitting, or walking about has been more marked and is present in all patients. The patients have been followed from six to 14 months. No blood pressure lowering was observed after the first thoracic operation in nine patients. This serves as somewhat of a control for nonspecific blood pressure lowering operative effects. The observed blood pressure lowerings seem to be related to the extensive removal of the sympathetic system.

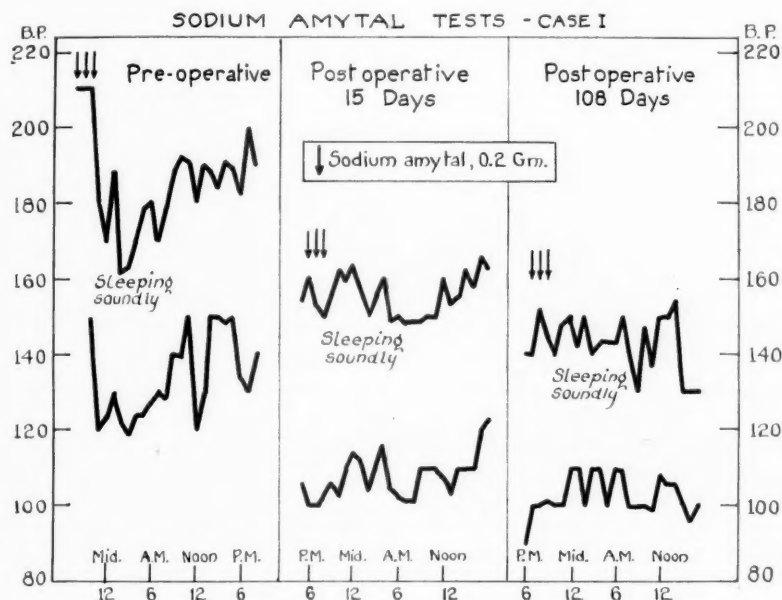


CHART 1.—Showing the effect of rest and 0.6 Gm. of sodium amytal during the 24-hour test periods on the blood pressure of Case 1, before the bilateral thoracic operation, and 15 and 108 days after this procedure. The general blood pressure level is lower. The sodium amytal test after operation produced no additional lowering.

Doctors Alving, Wright Adams, and others<sup>18</sup> have conducted extensive cardiorenal studies on many of these patients before and after operation. They have found no regular significant change in the urea clearance, the ability of the kidney to concentrate urine, venous pressure, or arm-to-tongue circulation time. The heart rate and cardiac output under basal conditions was decreased slightly. Studies of renal blood flow, glomerular filtration rate, and functioning tubular mass have shown no significant change. Renal blood flow increased in one patient and was either unchanged or decreased in the others. They conclude that such lowering of blood pressure as occurs after this extensive sympathectomy is due to a decrease in peripheral resistance. It is impossible at the present time to correlate this alteration of peripheral resistance to any alteration of possible etiologic factors in these patients that might parallel either experimental neurogenic or renal types of hypertension. The rôle that either or both of these factors, together with organic vascular pathologic changes increasing the peripheral resistance may play in clinical hypertension awaits further clarification.

## CONCLUSIONS

This is a report of studies in progress of the effect of extensive to total paravertebral sympathectomy in hypertension and no conclusions are drawn as to whether or not this operative procedure will prove to be one of lasting merit. It is a more extensive operation and carries a greater risk than does splanchnicectomy but it appears to lower the blood pressure more consistently. The results are sufficiently encouraging to warrant further studies of the cases already operated upon and further operative trial in selected cases.

The author wishes to acknowledge his appreciation for the cooperation and aid given by Drs. Alf S. Alving, Wright Adams, Jerome Gans, Louis Leiter, Richard Sternheimer, Alf Haerem and others, of the Department of Medicine who have cooperated in the study and management of these patients.

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DISCUSSION.—DR. R. H. SMITHWICK (Boston, Mass.): We have approached this problem from a rather different viewpoint than that which has been presented this evening. Our experience has been entirely confined to a study of hypertension in man. We have felt that hypertension in man, in itself, is a highly experimental and a very complicated problem. There appear to be a number of variable factors which combine to result in hypertension in man. I think there is one thing that we will all agree upon, and that is that nobody knows the cause of hypertension in man.

For this reason, we have felt that the best method of procedure was to start with the simplest operation that we thought might result in reduction of blood pressure. Because of the upright position of man, we have felt that the splanchnic bed must be much more highly developed, in order to maintain blood pressure relatively normal in the various positions than is the case with the dog. Therefore, we thought that it would be advisable, following the lead of Adson and Peet, to denervate the splanchnic bed and to see what the results of that procedure were and, if we found evidence from our studies that further surgery was indicated, to proceed on the basis of evidence derived from our studies in man, rather than from evidence deduced from experimental work.

A chart was shown by the speaker which represented what he considered a good result from partial denervation of the splanchnic bed. Our criterion for partial denervation of the splanchnic bed is that there is no significant change in blood pressure as the patient changes position. Our criterion for complete denervation of the splanchnic bed is a striking and precipitous fall in blood pressure as man shifts from the horizontal to the vertical position.

This patient is characteristic of the good results that we obtained, in a series of approximately 70 cases followed up to four years, by partial denervation of the splanchnic bed by one method or another. This happens to be the result of a supradiaphragmatic splanchnicectomy by the Peet technic. The patient is in the early stage of the disease, is very young, and fulfills all the qualifications that we know of that would indicate a good result. Her blood pressure has been within normal limits, except for possibly slight diastolic hypertension, for approximately four years. One might wonder what further effect there would be if this patient were totally sympathectomized. Our feeling has been, and we have been interested in the question of more extensive sympathectomy for a number of years, that faced with a result like this, in our present stage of ignorance concerning this disease, we were not justified in proceeding with further denervation.

In these 70 cases of partial denervation of the splanchnic bed, our medical department came to the conclusion that nine and one-tenth per cent had results comparable to this; that is, unquestioned persistent and significant lowering of blood pressure. That figure is considerably lower than has been reported by others, with much greater experience.

Some patients do not respond to partial denervation of the splanchnic bed, and in these, we wondered whether further denervation, more extensive sympathectomy, might be helpful. A chart was here shown of a patient who was one of a number of failures of partial sympathectomy, and decided to proceed further. First of all, before any surgery, she was followed in the out-patient department for several months, and while under observation developed an hemiplegia. She recovered from that satisfactorily, was followed several months more, and we decided to operate. She had a supradiaphragmatic splanchnicectomy in two stages, again the Peet technic. We felt there was no significant blood pressure response following the operation.

We decided to proceed further. I might say that in other cases before this, instead



of proceeding downward, as we did in this case, we proceeded upward, in order to increase the magnitude of the operation to include the lower half of both thoracic sympathetic chains, not including the heart. In no case who had failed to respond to the Peet operation did we get any significant response by proceeding higher in the thorax. On the other hand, by proceeding downward, we did, in a number of cases, observe a significant response. In other words, by adding bilateral lumbar sympathectomy in two stages we derived a significant response. Thus, in addition to the Peet operation, the first, second, and third lumbar ganglia were removed on both sides.

So we came, after a period of trial and error, to feel that complete splanchnicectomy, which resulted in postural hypotension in every case, might offer more for some of these individuals, and this was accomplished by removing the sympathetic trunks from  $D_6$  to  $L_1$  or  $L_2$ , inclusive, both sides, together with excision of the great splanchnic nerves from the semilunar ganglia to about the midthoracic level.

A chart was here shown demonstrating a typical good result from this procedure, showing a reduction of blood pressure to normal for two years in a patient with malignant hypertension.

We also wondered whether in patients who did not respond to the combined supra- and intradiaphragmatic operation further sympathectomy would be beneficial. A chart was here shown of a patient who had been sympathectomized totally. This was undertaken in seven stages, and we felt there was no significant response.

Our impression is that in patients who do not respond to complete splanchnicectomy, further denervation probably will not result in significant lowering of blood pressure. On the other hand, we feel that in those who do respond to complete splanchnicectomy, we are not justified in proceeding with further sympathectomy in the present state of our knowledge. Such indications may arise in time, but it is our notion that they had best be deduced from the study of hypertensive patients rather than from experimental animals.

Our percentage of significant and persistent lowering of blood pressure following complete splanchnicectomy, as contrasted with partial splanchnicectomy, is as 65 per cent is to 9.1 per cent, at the present time.

In commenting upon the paper this evening, I think we have been presented with a very detailed and valuable study in a small series of patients. It is difficult to compare this statistically at this time with other larger series. However, I think that Doctors Grimson and Phemister are to be congratulated on the care and the detail with which they have studied their cases. I think that time alone will tell whether total sympathectomy has anything more to offer these patients than less than total sympathectomy.

DR. GEORGE M. CURTIS (Columbus, Ohio): From carefully controlled clinical studies such as these, and particularly from those which have grown out of previous laboratory experimentation, much clinical physiology may be learned in evaluating the effects of the application of newer operative procedures. Thus the application of pneumonectomy to the treatment of lung carcinoma has led to the operating table demonstration of the low blood pressure normally present in the pulmonary artery.

In sympathectomy combined with ganglionectomy in the treatment of hypertension, we are thinking mainly of vasomotor effect, although secretory effects, and particularly those from the adrenal, have received due consideration. Nevertheless, other visceral mechanisms are also involved when the lower thoracic sympathetic chain and splanchnic nerves are removed. Thus, there is an ensuing increased motor activity of the stomach, perhaps due to the then unopposed action of the vagi (*Arch. Surg.*, **32**, 577, 1936).

However, we should be careful not to lose sight of the sensory fibers from the upper abdominal viscera. Some of these pass upward through the splanchnic nerves, along the ganglionated cord and through the white rami to the dorsal ganglia and spinal cord. In this surgical field, opportunity is thus afforded to learn something of the sensory impulses they carry. It may be that they act in an important manner in the sensory defense of the upper abdomen.

Thus a number of clinical symptoms are closely associated with hypermotility of the human stomach. Among these may be mentioned nausea, upper abdominal distress, or cramps, and certain types of "gas pains." Moreover, hypermotility may be induced by morphine with the production of upper abdominal distress and then controlled, together with the discomfort, by atropine.

Yet in the hypermotility subsequent to bilateral splanchnic resection, our few patients have not noted these accompanying disturbing sensations, such as would ordinarily accompany such evidence of increased gastric activity. Is it possible that excision of the splanchnic nerves has also removed an important sensory mechanism in the interpretation of visceral change in the upper abdomen? The answer to this question obviously has a practical clinical bearing and merits further clinical attention. Perhaps the speaker may also have a solution to the problem.

Our own consideration of the matter may be presented by showing a few charts:

Chart 1 shows the method which we have used for studying the motor activity of the human stomach following unilateral and bilateral splanchnic resection. The ink writer here obviates the smoked drum and makes this work possible in the clinic along with the white linen.

This is a roentgenogram showing the position of the balloon in the stomach, connecting through this tube to the kymograph.

Chart 2 is that of a patient, with an obstructive duodenal ulcer, showing a marked increase in gastric motility, and with it was associated severe abdominal pain. Later, ensued a spontaneous remission of the increased motility with cessation of the upper abdominal distress.

Chart 3 is that of a patient who had, postoperatively, what are commonly called "gas pains" or cramps, and as these occurred he pressed a button, recording these simultaneously with increases in peristaltic action of the stomach. Atropine intravenously, 1/150 gr., at this point was given, with cessation of the distress and the associated increased contractions.

Chart 4 is that of patient with duodenal ulcer, to whom morphine, 1/8 grain intravenously, was given at this point. Note the ensuing increased activity, both in frequency and amplitude. This was accompanied by definite upper abdominal distress. After giving atropine, 1/150 gr., intravenously, there ensued cessation of the increased motility and disturbed sensation. Then prostigmine 1 to 2,000 was given at this point, which reversed the atropine effect and induced motility again. This increased in amplitude and frequency and its occurrence was accompanied by pain. Ephedrine at this point decreased the motility with an accompanying disappearance of the uncomfortable sensation. Thus, we would think that associated with gastric hypermotility there is usually abdominal pain or distress or discomfort (*Trans. West. Surg. Assn.*, pp. 447-475, 1938).

Chart 5 is that of a patient who had previously had a resection of the left splanchnic nerves and later of the right splanchnic nerves. This operation, after the technic of Peet, was undertaken in two stages. Subsequent to this, there occurred a marked and persistent hypermotility of the stomach. You see here the increase in amplitude and frequency, which lasted for five hours. We have seen this increased activity persist for a period of six hours, with no complaint of discomfort or of other sensations ordinarily associated with hypermotility, whether occurring spontaneously or induced by morphine. This is another curve made from this same patient. Note the increase in amplitude of the peristaltic waves. Yet this patient did not complain of upper abdominal distress at that time (*Am. Jour. Physiol.*, 120, 356, 1937).

Chart 6 is that of a patient in whom a bilateral splanchnic resection was performed, according to the Peet technic. You see ensuing increased gastric motility. Yet with this hypermotility there was likewise no upper abdominal distress.

Thus, it would appear that the splanchnic nerves carry certain visceral sensations to the central nervous system, and that these are interrupted and, consequently, not interpreted following bilateral splanchnic resection. The clinical import is obvious, and further consideration seems warranted.

DR. MAX M. PEET (Ann Arbor, Mich.): I believe that we ought to study our hypertension patients, both before and after operation, from every standpoint, not just blood pressure. We ought to know the changes in the retina, the changes in the kidney, and in the heart. So we have studied all our patients from every possible standpoint. We have felt, as the others have, that the work is still experimental in many ways, and we could best determine its actual value by using one particular surgical procedure. We have operated upon some 700 patients now, using a bilateral supradiaphragmatic splanchnicectomy with the resection of a long segment of the greater splanchnic nerve and excision of the tenth, eleventh, and twelfth thoracic sympathetic ganglia. Often when pulling up on the greater splanchnic, we actually see the top of the celiac ganglion.

The excised portion of the greater splanchnic nerve extends from the eighth or ninth vertebrae to the diaphragm and measures, after removal, 10 to 15 cm. in length. Excision of such a long segment probably prevents regeneration. Occasionally, the ninth thoracic ganglion is readily exposed and when this occurs it is removed with the tenth and eleventh. Sometimes, the twelfth is deeply imbedded in the diaphragm, making its excision impossible. Under such circumstances, we have always cut the twelfth ramus, even though the exposure of this ramus required rather extensive division of the vertebral attachments of the diaphragm.

To rule out possible differences in individual technic, all the patients included in our very thorough follow-up studies were operated upon by me. All have been studied preoperatively and again at a minimal postoperative period of at least nine months by the medical, cardiac, ophthalmologic, and roentgenologic departments of the University Hospital. Pre- and postoperative studies included blood nonprotein nitrogen, water concentration, and urea clearance determination, electrocardiograms, orthodiagrams, and teleoroentgenograms, fundusoscopic examinations, and numerous blood pressure readings from both arms.

Only by such a thorough study can we evaluate any therapeutic procedure. Many of our patients have been studied repeatedly for several years. The longest postoperative period studied in any one patient, a man who before operation had a severe malignant hypertension, is seven years.

I submit the following tables from a paper on the Surgical Treatment of Hypertension, by Peet, Woods, and Braden (J.A.M.A., 115, 1875-85, November 30, 1940), to show you some of the results of bilateral supradiaphragmatic splanchnicectomy. I believe these are as good as those obtained by the much more formidable procedure of total or subtotal sympathectomy. The latter cannot as yet be definitely evaluated since the series is small, complete studies have not been made, and too short a postoperative period has elapsed:

TABLE I  
BLOOD PRESSURE

	Number	Per Cent
Cases studied nine mos. or later postoperatively (including deaths) . . . . .	290	100
Reduced (more than 40 Mm. systolic and 15 Mm. diastolic) . . . . .	149	51.4
Unchanged . . . . .	134	46.2
Increased (more than 10 Mm. systolic and 5 Mm. diastolic) . . . . .	7	2.4
Cases with no data or dead before nine mos. postoperatively . . . . .	63	

If the 60 patients concerning whom no data were obtained or who died before nine mos. are considered as unchanged or worse, the percentage of patients with significantly reduced blood pressure in the whole group of 350 cases becomes 42.6.

Table I shows the results of splanchnicectomy in a series of 290 patients followed from nine months to seven years. We have not considered any patient under nine months. You notice that of 290 consecutive patients 149, or 51.4 per cent, have had a reduction in blood pressure of more than 40 Mm. systolic and 15 Mm. diastolic; 46 per cent were unchanged. It is possible that some of the latter might be improved further by either a higher thoracic or a lumbar ganglionectomy. Only 2 per cent have increased here.

TABLE II  
ANALYSIS OF PATIENTS WITH SIGNIFICANTLY REDUCED BLOOD PRESSURE

	Number	Per Cent
Number of cases studied . . . . .	149	100
Reduced to normal . . . . .	56	37.5
(130/90 for ages 20 to 40)		
(150/100 for ages 40 to 70)		
Markedly reduced (but not to normal) . . . . .	15	10.1
(More than 80 Mm. systolic and 25 Mm. diastolic)		
Reduced (but not markedly or to normal) . . . . .	78	52.4
(More than 40 Mm. systolic and 15 Mm. diastolic)		

Thus, of those cases in which there was significantly reduced blood pressure 47.6 per cent were reduced to normal, markedly reduced or both.

Of the 149 cases that showed worth while reduction, 37 per cent have had reductions to what our medical department considered normal. In other words, these patients

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have had a normal blood pressure at a postoperative period from nine months to seven years. Certainly this group of patients, representing 37 per cent of those with a significant reduction in blood pressure, did not need a more extensive sympathectomy.

The blood pressure was considered as markedly reduced but not necessarily to normal, if the reduction was more than 80 Mm. systolic and 25 Mm. diastolic. These constitute 10 per cent. Those reduced more than 40 Mm. systolic and 15 Mm. diastolic but not markedly or to normal, constitute the remaining 52 per cent. It is significant that nearly half of those with a reduction in blood pressure had such a striking result as to be classed as either markedly reduced or reduced to normal.

I might remark that all the preoperative readings were made while the patient was quiet, usually in bed, while the postoperative readings were made while the patient was active and going through various tests. There is no postural change in blood pressure after supradiaphragmatic splanchnicectomy and resection of the lower thoracic sympathetic chain.

As stated before, we not only study the blood pressure but also the eye changes, cardiac condition, renal function, symptomatology, and ability to work.

TABLE III

SUMMARY OF RESULTS OF SPLANCHNICECTOMY: PERCENTAGE OF CASES STUDIED SHOWING IMPROVEMENT (FROM NINE MONTHS TO SEVEN YEARS AFTER OPERATION)\*

	Per Cent
Blood pressure	
Reduced to normal.....	11.7
Markedly reduced (but not to normal).....	7.6
Total cases significantly reduced.....	51.4
General disability	
Symptoms improved.....	86.6
Complete recovery incapacitation.....	55.5
Total cases with improvement incapacitation.....	81.3
Eyegrounds	
Disappearance of papilledema, when present.....	73.8
Total cases with improvement.....	69.4
Heart	
Heart size diminished.....	64
Electrocardiogram improved.....	53.4
Renal function	
Urea clearance improved.....	52.2
Urine concentration improved.....	44.8

\* Statistics include those patients who showed improvement but who subsequently died.

Table III shows a summary of 350 consecutive hypertensive patients treated by bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy. Fifty-one per cent had a worth while reduction in blood pressure. Symptoms were improved in 86 per cent. Papilledema was absent in 73 per cent of those who had choked disks before operation. Heart size was diminished in 64 per cent. The kidney function was improved as follows: Water concentration, 44.8 per cent; urea clearance, 52 per cent. Complete recovery from incapacitation occurred in over 55 per cent.

If we are going to evaluate any procedure for the treatment of hypertension, we must show not only improvement in blood pressure but improvement in heart size, in kidney function, and in other ways. Bilateral supradiaphragmatic splanchnicectomy certainly fulfills these requirements as shown by the above statistics.

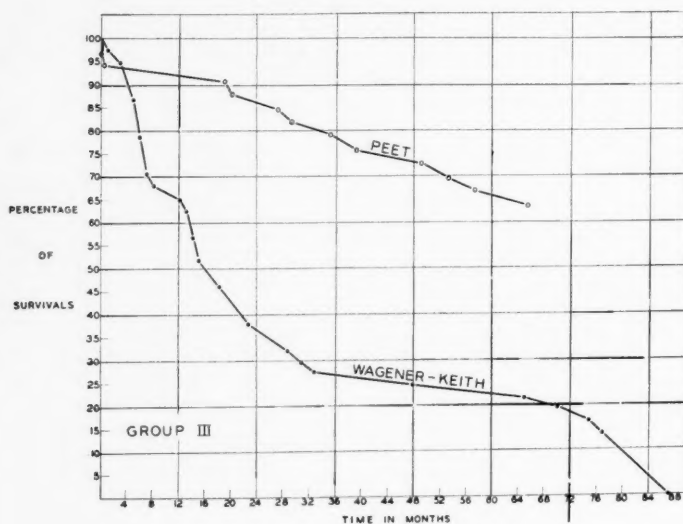
Recently we have compared our mortality after a five- to seven-year postoperative period with the Keith-Wagener table of similar patients treated medically. These cases have been grouped according to the preoperative ocular findings. Graphs 1 and 2 are from a paper by Woods and Peet which will appear in the Journal of the American Medical Association.

Group III represents a very serious type of hypertension manifested by spasm of the retinal arteries, hemorrhages, and often exudates. It will be noted in Graph 1 that the mortality in Group III when treated medically is very high. The same group when treated by splanchnicectomy has a much lower mortality.

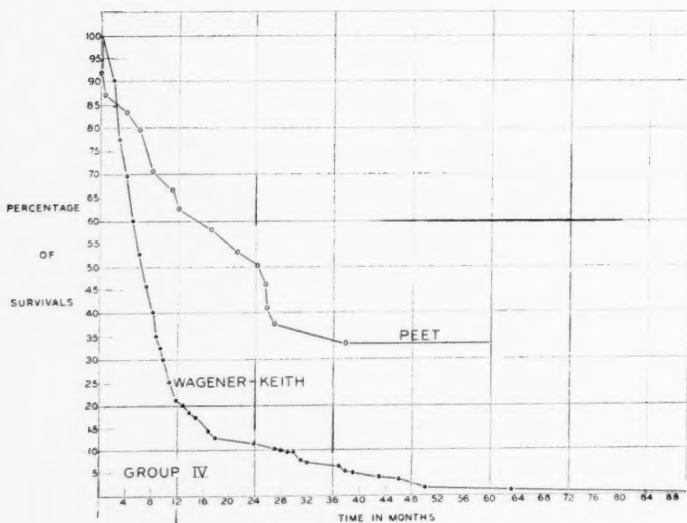
Group IV (Graph 2) represents the so-called malignant type of hypertension and is manifest by papilledema in addition to the retinal changes found in Group III

(Graph 1). The patients in this group have an exceedingly poor prognosis. It will be noted in Graph 2 that the majority of these patients died within the first year under medical treatment. The mortality in the surgical group is much higher than in any of the other groups treated surgically, but is much more favorable than the corresponding medically treated group.

I believe the data here submitted demonstrates the value of bilateral supradiaphragmatic splanchnicectomy, with resection of the lower thoracic sympathetic ganglia.



GRAPH 1.



GRAPH 2.

DR. ALFRED ADSON (Rochester, Minn.): About ten years ago, I was prompted to devise a procedure to alter the blood pressure of patients suffering from essential hypertension. The operation was based on the principle that blood pressures decrease when high spinal anesthesia is employed. The intent was to reproduce changes similar to



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those that occur at the time spinal anesthesia is produced. It consisted of bilateral ventral rhizotomy which included the roots on both sides from the sixth thoracic to the second lumbar vertebrae inclusive. It was performed for the specific purpose of interruption of the vasomotor nerves in the hope that such a procedure would relieve peripheral resistance due to vasospasm. Fortunately, some satisfactory results were obtained. The magnitude of extensive laminectomy and rhizotomy stimulated me to alter the procedure in order to make it less shocking. The next procedure that I devised is bilateral subdiaphragmatic, extraperitoneal resection of the splanchnic nerves with the portion of the celiac ganglion and removal of the lumbar sympathetic trunks, including the first and second lumbar ganglia.

The results of this operation appeared to be equally as good as those that followed extensive rhizotomy. However, it soon became apparent that not all patients responded equally well to the operation. Those who obtained the best results were those whose blood pressure receded to near normal values on rest in bed and who received sodium amyltal prior to operation. It also became apparent that the relief of clinical symptoms often was greater than the actual reduction of blood pressure. Patients who had beginning arteriosclerosis and those who already had sustained irreparable damage to the cardiorenal system obtained only temporary or no relief from extensive sympathectomy.

Although various approaches and procedures are employed to interrupt the vasomotor control of a large vascular region, the problem of surgical treatment still remains one of experimentation since Goldblatt, Page, and many others have shown that ischemia of the kidney with the resulting development of a vasopressor substance results in a state of hypertension that is not amenable to sympathectomy. Until such time that an antipressor substance can be produced and administered with safety, I believe we are justified in continuing extensive sympathectomy. It should not be employed indiscriminately in the light of our experiences. May we hope that the operation suggested by the essayist will be more effective than those operations that are being employed.

DR. LOYAL DAVIS (Chicago, Ill.): As Doctors Grimson and Smithwick have pointed out, the question of hypertension is a very difficult one and none of us knows all of the exact factors involved in its production. For this reason, it is important that we have a good understanding of what essential hypertension means to each of us before we can understand one another and our results. For us, the term "essential hypertension" includes those cases of chronic hypertension which neither clinically nor anatomically can be demonstrated to have evolved from an antecedent inflammatory disease of the kidneys or from urinary obstruction. In addition to a high systolic and diastolic blood pressure, the changes in the blood chemistry and the clinical stages of the disease are the important factors which must be studied.

In our own experience, the majority of patients with essential hypertension react favorably to the correct administration of potassium sulphocyanate, but there is a group of patients who are resistant to the cyanates and it is to this group that we have devoted our attention in an attempt to do something for them surgically. We have reported upon the fact that many of the patients who are resistant to the cyanates become sensitive following a bilateral supradiaphragmatic splanchnicectomy. In our second series, we are now performing a supra- and infradiaphragmatic section of the splanchnic nerves and removal of the first two lumbar sympathetic ganglia. As yet, it is too early to report upon the results in these patients but we have the impression that this combined operation is more effective.

We are interested in knowing whether or not Doctor Grimson's experimental animals showed an increase in the hematocrit reading, blood protein, and cholesterol levels in addition to their high blood pressures. This is true of the hypertension produced experimentally by ischemia of the kidneys, and, in our opinion, must be present to be correlated accurately with hypertension in man. In our own laboratory, we were able to produce hypertension in the same manner as has Doctor Grimson, but the blood chemistry studies on those animals were never analogous to the blood chemistry findings in clinical hypertension.

It is only by adding together all of the results from the various surgical procedures which are being carried out on man and the experimental investigations, that we will be able to come to some understanding about a problem which is a very difficult one.

DR. NORMAN E. FREEMAN (Philadelphia): I have been following the work of Doctors Grimson and Phemister with great interest. In our own studies, we were first interested in attempting to prevent the renal type of hypertension by sympathectomy. Four years ago, Doctor Page and I found, just as Doctors Grimson and Phemister have found, that total sympathectomy, including cardiac denervation, did not prevent the rise in blood pressure produced by constriction of the renal artery in the dog.

Three years ago, with Doctor Jeffers, I undertook some experiments on how little of the sympathetic nervous system it was necessary to remove in order to prevent the reflex nervous hypertension which took place from raising the intracranial pressure. We found, as Doctors Grimson and Phemister found, that upper thoracic or lower thoracic sympathectomy alone did not prevent it, but when we combined the two or performed total sympathectomy, the rise in blood pressure from raising the intracranial pressure could be prevented.

On analyzing our results further, we finally found it was necessary to remove only the sympathetic nerves from the heart and to exclude reflex nervous adrenal secretion in order to prevent this type of hypertension. In other words, we could leave in both sympathetic chains from the sixth thoracic to the fifth lumbar, provided we had excluded the adrenal secretion, either by taking out one adrenal and denervating the other, or taking out one adrenal and injecting novocain into the medulla of the other gland.

It would seem from the analogy of the development of malignant hypertension in patients and malignant hypertension in dogs after constriction of the renal artery, that there is a close relationship between the experimental hypertension of Goldblatt and clinical hypertension. On the other hand, I do not think that the nervous influence has been excluded. I think it may be possible that the nervous influence produces its effect by way of renal vasoconstriction. In our own clinical work, we have followed the technic of thoracolumbar sympathectomy, suggested by Smithwick, in order to provide as complete as possible a sympathectomy of the renal area.

DR. GEORGE J. HEUER (New York, N. Y.): In view of the references to the effects of various surgical methods of treatment made by other speakers, I should like to refer to the results we thus far have obtained with the operation of anterior root section. In 19 patients with essential hypertension, five or more years have elapsed since we performed this operation and we are, therefore, in the position of stating the five-year results obtained. When we consider the course of the disease, its progressive nature, its eventual outcome, its tendency to recur, if I may so speak of it, after operative treatment, we may liken it to malignant disease; and in appraising methods of treatment we should hesitate to speak of results which have not extended over a five-year period. Of the 19 patients operated upon, five or more years ago, 12 are dead. Of the 12, two lived to within a few months of five years, one lived almost four years, one lived three years, and the remaining eight from a few months to one and one-half years. Of the 12 dying, five died as a direct result of cerebral hemorrhage, seven died of cardiac disease associated with uremia. While these patients lived, four showed marked improvement in their subjective symptoms; others showed moderate improvement. With respect to their blood pressures (last observations before death), two showed the same systolic and diastolic pressure as before the operation; and ten showed a reduction in both systolic and diastolic pressure. The reduction in systolic pressure varied between 20 and 90 Mm.Hg., and averaged 50 Mm.Hg.; the reduction in diastolic pressure varied between 20 and 40 Mm.Hg., and averaged 27 Mm.Hg. When one studies the causes of death it would seem, in this group, that such reduction in blood pressure did not alter the course of the disease.

Of the seven patients in this series who are now living, all are alive six years, and six are alive from six to seven years after operation. They have all been examined recently. They appear to be in remarkably good condition. They are free from the subjective symptoms they previously had, and are all active and following their usual occupations. With respect to their blood pressures, in two, the blood pressures are normal; in three, elevated (systolic 180, diastolic 105); in two, definitely elevated (systolic 210/220, diastolic 100/120). It would appear that in some of these patients the course of the disease has been interrupted and life prolonged; but it is clear that even a longer period of observation is necessary before final results can be stated with assurance.

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DR. KEITH S. GRIMSON (Chicago, closing): I am not in position to discuss the effect upon hypertension of splanchnicectomies of the various types. There have been more than 1,800 operations of this type performed and, as time goes along, an accurate postoperative study should properly evaluate the procedure. The high incidence of indifferent results reported after splanchnic area denervation, and the marked experimental difference between partial and total sympathectomy have led to the operation of total paravertebral sympathectomy in man. It is hoped that better results may be obtained by this procedure.

I believe that the discussers have brought out the differences of opinion concerning the various types of splanchnicectomy, and, of course, the medical men have still further differences of opinion. Studies of hypertensive patients are very difficult to control, and there has been considerable controversy about the effect of splanchnic area denervation. We have had little experience with this operation.

Doctor Curtis asked about gastric motility and sensation. This operation, as it has been performed, includes the celiac ganglia, in an effort to prevent regeneration. Motility studies have shown no abnormality. It is surprising how well patients can get along without the sympathetic system.

Doctor Davis asked about thiocyanate therapy. That has not been given to these patients postoperatively because as yet we have not felt that they have needed it. There is one exception. That is the patient I first spoke of, who had had a period of thiocyanate with no result; sympathectomies with very indifferent results; and then sulphocyanate—again, with still no result. There certainly is a chance that the peripheral resistance may have become so fixed in this patient that no mechanism which can be attacked is going to relax it.

I have not time to go over all of the discussion, except to say that we do fully recognize that these results are very early. We report them in the interest of an attempt to get at the mechanism of the hypertension, and in the hope that perhaps more might be accomplished by this procedure than by partial sympathectomies.

## ASCORBIC ACID AND HUMAN WOUND HEALING\*

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DURING the last few years, surgeons have been paying increasing attention to all the circumstances that play a part in the successful healing of operative and other wounds. The mechanical factors involved have been studied in great detail by two groups led, respectively, by Harvey,<sup>1</sup> and Whipple.<sup>2, 3</sup> Harvey, in particular, has shown how much strength can be expected in a given wound, at a given time, with a given type of suture material, properly placed. Eighty per cent of the disruptions that formerly occurred in Whipple's clinic have been avoided by changes in technic. Very widely over the country, there has been a steady shift in technic toward finer suture materials and especially toward fine silk and cotton, and to more suitable placing of sutures. With this change, better results are certainly being achieved.

During the same period of time, two chemical factors, plasma protein and ascorbic acid, that effect healing, have also come into prominent attention. Harvey showed an increased rate of healing on a high protein diet. Whipple,<sup>4</sup> Carrel,<sup>5</sup> and Ravdin,<sup>6</sup> have shown that a slight degree of lowering of the level of plasma protein may delay healing. A marked lowering will delay it enough so that even the most meticulous care in the type and placing of sutures may not result favorably.

More recently, the importance of ascorbic acid has been recognized in wound healing. Lanman and Ingalls,<sup>7</sup> Archer and Graham,<sup>8</sup> and Ingalls and Warren<sup>9</sup> made the earliest observations on surgical patients in which plasma ascorbic acid determinations were made. Lanman and Ingalls,<sup>7</sup> and also Taffel and Harvey<sup>10</sup> have studied the tensile strength of experimental wounds in animals with scurvy. Partial scurvy delays healing in animals. More recently, Wolfer and Hoebel,<sup>11</sup> Bartlett, Jones, and Ryan,<sup>12</sup> Holman,<sup>13</sup> Hartzell, Winfield, and Irwin,<sup>14</sup> and Lund and Crandon<sup>15</sup> have made further observations on man. All of these authors have found that many of their patients have subsaturation levels of ascorbic acid in the plasma. Some of them offer the opinion that a low plasma ascorbic acid level indicates a degree

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of deficiency that may cause failure of healing. Crandon, Lund, and Dill<sup>16</sup> showed that slight or even moderate deficiency in ascorbic acid reserves did not effect the healing of an experimental wound in a human. They also showed that plasma ascorbic acid determinations were not a good index of deficiency and that the plasma vitamin C level could be zero, and yet the patient might be far from having clinical scurvy, and his wound might heal quite normally. This indicates that the vitamin C reserves in the tissues or in the tissue cells and not the level in the plasma are the determining factor for healing. They also confirmed the finding of Butler and Cushman,<sup>17</sup> and showed that ascorbic acid determinations, made on leukocytes, gave a much more certain evidence of the degree of depletion of the body reserves of this substance. If the leukocyte level is below 4 mg. per 100 Gm., we consider the patient to be close to scurvy. (The normal value is 30-40 mg. per 100 Gm.)

Another method of studying the reserves of ascorbic acid is by saturation tests. Such tests may be carried out by measuring the plasma levels, the urinary excretion, or both, before and after test doses of the vitamin which may be given either by mouth or intravenously. Studies of the degree of ascorbic acid deficiency, by making saturation tests, have been made by many investigators. Wright, Lilienfeld, and MacLenathan,<sup>18</sup> Wright and MacLenathan,<sup>19</sup> and Portnoy and Wilkinson,<sup>20</sup> are among those whose data are very useful. Crandon, Lund, and Dill also performed a saturation test at the completion of their experiment, and determined the changes in the plasma and leukocyte ascorbic acid levels as scurvy was relieved. It is the authors' belief that one of the best and simplest saturation tests is performed by making daily plasma determinations 24 hours after daily doses of 1 Gm. of the vitamin given either intravenously or by mouth. Tested in this way, a moderately severe case of scurvy showed a zero level in the plasma the day after the first dose, 0.1 mg. per 100 cc.; after the second, 0.4 mg.; after the third, 0.6 mg.; after the fourth; and 0.8 mg., after the fifth dose. The leukocyte ascorbic acid determinations on the first four days showed 3, 15, 30, and 32 mg. per 100 Gm., respectively. Other cases studied by us failed to show any rise in the plasma level until after the fourth dose. Other laboratories have made similar findings. Provided intestinal absorption is normal it makes little difference whether the test dose is given by mouth or intravenously. Doses of ascorbic acid in smaller amounts may also be given. In some of our earlier work, various doses of less than 1 Gm. were tried. A good idea of the vitamin deficiency may be gained by such doses, but the period of testing is prolonged.

It is always preferable to know what the levels are before treatment is started, but if one is sure of the doses given one can sometimes calculate the degree of deficiency without such information. For instance, if a patient had a plasma level of 0.3 mg. per 100 cc. the morning after the third daily intravenous dose of 1 Gm. of ascorbic acid, one can be quite sure that a severe deficiency was present at the start of the treatment.



Another way of estimating the amount of deficiency is to calculate the amount of the vitamin taken by the patient in his food. This is less accurate, much more troublesome and more time-consuming than other methods, but has the great advantage of being available to any doctor and not necessitating any very delicate, expensive laboratory tests.

Dietary histories were taken on all the cases reported below. To evaluate such data the vitamin content of the foods must be estimated by calculation. These calculations were made from the data in Vitamin Content of Foods.<sup>21</sup> We believe that patients may maintain fair but not saturated reserves with an intake of 25 mg. of ascorbic acid per day,<sup>16</sup> but that when an intake below 10 mg. has prevailed for a long time that the reserves probably become severely depleted.

Two developments of the same general nature, but different in degree, occur as a result of poor healing after abdominal operations. One of these is post-operative hernia—due to failure of the fascia—and the other is disruption which is due to failure of all layers of the wall to heal. Both of these developments have been studied.

*Postoperative Hernia Following Gallbladder Operations.*—Lund and Crandon showed that various plasma vitamin C levels had no relation to the development of postoperative pulmonary complications. Fifty-eight of the same patients presented in that study, returned to the Follow-Up Clinic from three months to one year after discharge, and were studied for the presence of postoperative hernia by one of us (J. H. C.). Nine herniae were found. These patients were then tabulated in the same way they had been when the study of pulmonary complications was made (Table I).

TABLE I  
VITAMIN C AND POSTOPERATIVE HERNIA FOLLOWING BILIARY OPERATIONS

Preoperative Plasma Ascorbic Acid—Mg. Per 100 Cc.....	Average Preoperative Diet in Mg. Per Day			Total
	25	10-24	10	
0.5.....	$\frac{1}{25} = 9\%$	$\frac{0}{0} = 0\%$	$\frac{0}{0}$	$\frac{1}{1} = 7\%$
0.2-0.49.....	$\frac{11}{9} = 11\%$	$\frac{3}{11} = 0\%$	$\frac{0}{1} = 100\%$	$\frac{14}{21} = 9\%$
0.0-0.19.....	$\frac{1}{6} = 17\%$	$\frac{1}{6} = 17\%$	$\frac{2}{6} = 33\%$	$\frac{4}{18} = 22\%$
Unknown.....	$\frac{1}{2} = 50\%$	$\frac{0}{2} = 0\%$	$\frac{1}{1} = 100\%$	$\frac{2}{5} = 40\%$
Total.....	$\frac{4}{28} = 14\%$	$\frac{1}{22} = 5\%$	$\frac{4}{8} = 50\%$	$\frac{9}{58} = 15\%$

The numerators of each fraction indicate herniae. The denominators indicate total cases in each group.

It is seen from Table I that those cases with low plasma levels in the blood preoperatively showed a larger percentage of herniae than did those with high levels. Likewise, those with small amounts of the vitamin in their diet had a larger percentage than did those with fair or large amounts. However, these statistics, while we believe them to be of some significance, must be interpreted with great caution because of the fact that low plasma

# WOUND HEALING

values do not always mean depleted reserves, and patients who indicate a low intake on dietary history are perhaps not always telling the truth. However, *all* the patients in the higher brackets should heal, in so far as ascorbic acid is a factor in their healing. On the other hand, *some* of the patients in the lower brackets may be near enough to scurvy to interfere with their healing. With this reservation, and with the further reservation that the group of cases is small, it is believed that these statistics are sufficiently significant to indicate that cases with a low level of vitamin C in the plasma, if not corrected promptly, have more postoperative herniae than those with higher levels.

*Disruption.*—Twelve cases of wound disruption have now been studied from the standpoint of surgical technic and vitamin C reserves. The study is much more detailed than that undertaken on the cases of herniae. The estimation of the reserve supply of vitamin C was not made by the same method in all instances, so each case will be discussed briefly. Very few cases were studied early in the work as we did not then know how to interpret our plasma vitamin C values in postoperative cases. No studies of plasma protein were made, but transfusions were administered freely in certain of the cases that would have been likely to have low plasma values.

The cases were operated upon by several different surgeons and various different technics of wound suture were employed. In all cases, catgut was used and in many cases the catgut was of much larger caliber (Nos. 1 and 2

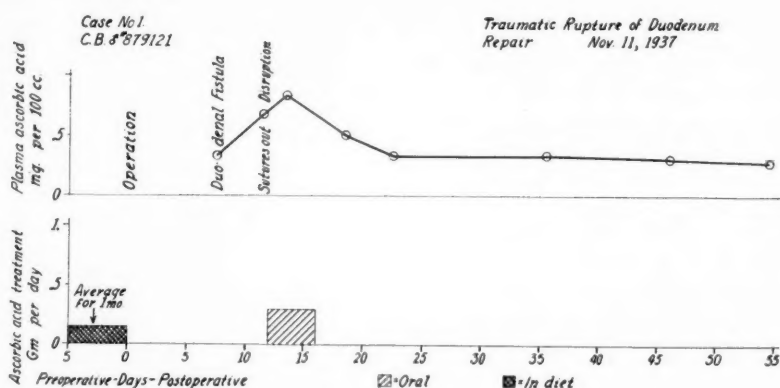


CHART 1.

chronic) than recommended by Whipple. Layer suturing, continuous to the peritoneum, and continuous or interrupted to the fascia, and silk or silkworm gut in the skin was the technic in all cases. A few silkworm stay-sutures were introduced in all cases. No overlapping or mattress sutures were used in the fascia. This technic in no way meets the standards set up by Whipple or Harvey, but the incidence of disruption was not believed to be excessive, although statistical studies to determine this incidence were not made. Three cases in this series have already been presented and discussed.<sup>15</sup> They are Cases 2, 4, and 6. Case 2 of the previous report is not presented again as

the peritoneum did not separate. In this report, only cases with complete separation of all layers are considered. The cases are presented in chronological order.

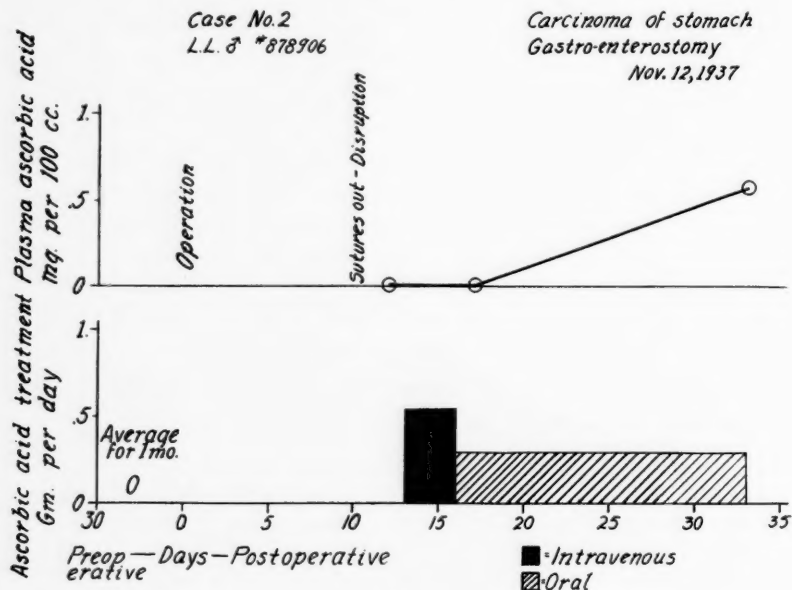


CHART 2.

**Case 1.**—*No Scurvy.* Hosp. No. 879121: C. B., a healthy high school boy, was injured playing football. He was brought to the hospital at once, and, at immediate operation, a traumatic retroperitoneal rupture of the duodenum was repaired with catgut. He had a stormy convalescence complicated by the early development of a duodenal fistula. Disruption occurred on the twelfth day, immediately after removing the stay-sutures. The wound was resutured. Chart 1 shows the intake and levels of plasma ascorbic acid. Calculations of the amount of ascorbic acid in the diet while in the hospital were not made as there was no possibility that this boy had scurvy. (See the high normal dietary intake before the accident.)

**COMMENT.**—Because of the high dietary intake and the plasma levels well above zero, we do not believe that vitamin C had anything to do with the disruption. Treatment of 0.3 Gm. per day was given because we did not then know that the levels determined were of no importance under these conditions. This disruption was due to technical factors and the chemical effect of duodenal secretion on the sutures. The boy eventually recovered.

**Case 2.**—*Near Scurvy.* Hosp. No. 878906: L. L., male, age, 59, had carcinoma of the stomach. His diet had contained very little, if any, ascorbic acid for months and he had lost 50 lbs. in weight. An exploration and anterior gastro-enterostomy were undertaken. Disruption occurred on the tenth day, shortly after removal of the stay-sutures. The wound was resutured and healed well.

**COMMENT.**—The preoperative diet was such that a condition close to scurvy was likely. After four days of 0.6 Gm. of ascorbic acid, intravenously,

# WOUND HEALING

the plasma level was still zero. After 17 further days of treatment by mouth, with daily doses of 0.3 Gm., the level was only 0.6 mg. per 100 cc. Inasmuch as there was no fever, sepsis or gastro-intestinal disturbance, these figures can only mean that this man probably had ascorbic acid deficiency of severe enough degree to contribute to this disruption.

**Case 3.**—*No Scurvy.* Hosp. No. 932411: T. A. D., male, age 45, with a gastro-jejunal ulcer of considerable duration. Vitamin deficiency was suspected and the ascorbic acid deficiency treated preoperatively, by giving 1.0 Gm. per day for three days. Determinations on two days showed a normal level. A difficult gastric resection and

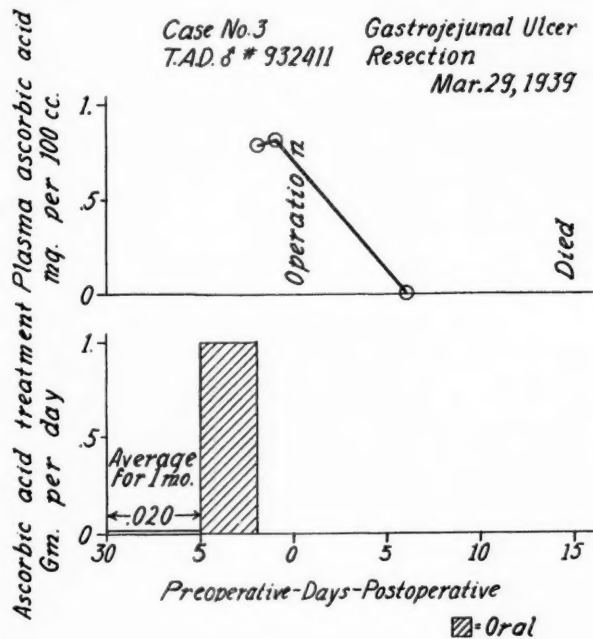


CHART 3.

repair was performed. On the third day, there was noted severe wound sepsis. Other complications followed, including hemorrhages from the wound and the stomach. Some delay occurred before treatment with vitamin K was given, as we did not, at that time, suspect that this deficiency was possible in such a case. In spite of treatment with vitamin K and many transfusions, the man died of peritonitis. Autopsy showed complete separation of the wound with a loop of intestine presenting just below the separated skin.

**COMMENT.**—Vitamin C played no part in this disruption, which was probably due, mainly, to effects of infection on the catgut sutures.

**Case 4.**—*Probably No Scurvy.* Hosp. No. 939296: R. F., male, had an appendix abscess. Until ten days before admission, and 20 days before operation he had had a diet fairly adequate in ascorbic acid (about 40 mg. a day). The operation consisted of drainage of the abscess through a right rectus incision. Disruption and protrusion of loops of intestine occurred 33 days after operation.

The data concerning vitamin C is relatively scanty. Two days before the operation,

and on the fifteenth day after it, the plasma level was zero. No vitamin C was given before the disruption. The convalescence was very stormy. Practically no food was taken for three weeks after the operation during which time Wangenstein drainage was constant. Fever was present from before admission to after the disruption. Eventually he recovered.

COMMENT.—No studies, that we know of, allow us to predict how long it takes for scurvy to develop in the presence of severe infection. All the evidence points toward the time being much shorter than without infection. The main cause of this accident was undoubtedly sepsis. Usually, in such cases

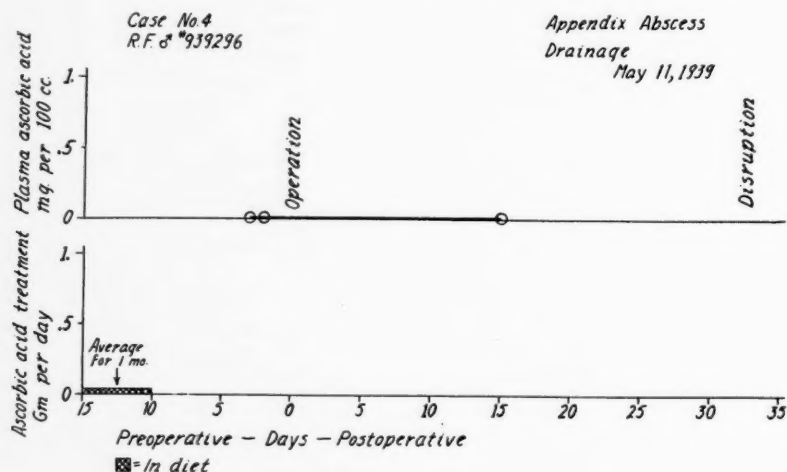


CHART 4.

firm adhesions prevent protrusion of the intestines, even if the wound breaks down. Possibly, there was a factor of vitamin C deficiency developing late in the infection, but the conservative position to take is that this case probably suffered from no important deficiency in spite of the zero plasma levels.

**Case 5.—No Scurvy.** Hosp. No. 944466: M. T., a male, had a ruptured gastric ulcer and was operated upon promptly. On the tenth day, the stay-sutures were removed and his wound disrupted a few hours later. Four days later, his ascorbic acid level was found to be 0.1 mg. per 100 cc. The morning after the first dose of 1 Gm. of ascorbic acid the level was 0.4 mg.

Comment.—This finding indicates that vitamin C was not a factor in this case of disruption.

**Case 6.—Near Scurvy.** Hosp. No. 970288: M. A. had had a duodenal ulcer for a long time, and severe obstruction for months. He had also been a heavy user of alcohol. He had been able to retain very little of the nourishment taken by mouth for some time before operation and he had lost 50 lbs. in weight. The surgical service had understood that plenty of ascorbic acid had been given before the operation, as preparation for it, but nobody realized how completely all food and vitamins taken by mouth had been vomited.



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After operation, his stay-sutures were removed prematurely on the sixth day. The wound promptly disrupted. No tablets of ascorbic acid were used, but from the second day after the disruption over a pint of orange juice was taken daily along with his food and he retained it all. This was equivalent to about 200 mg. per day. The laboratory

Case No.5  
M.T. ♂ #94466

Perforated Gastric Ulcer  
Suture—June 21, 1939

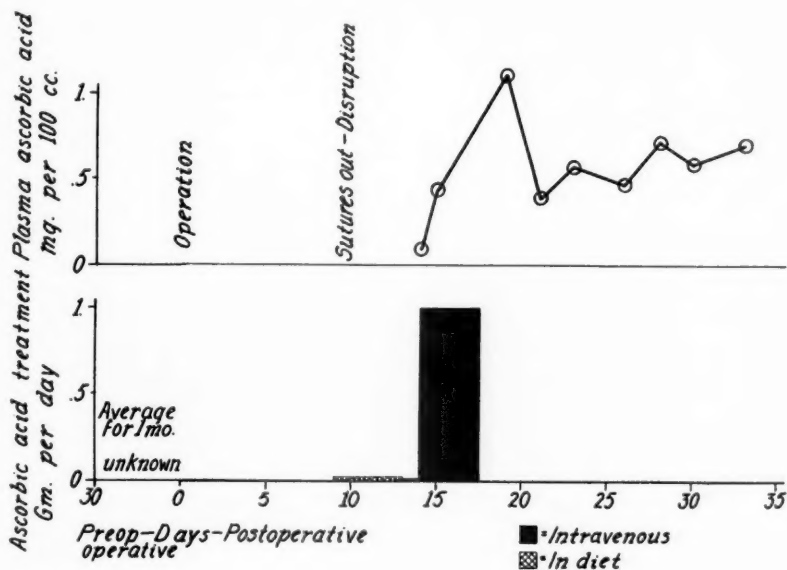


CHART 5.

Case No.6  
M.A. ♂ #970288

Obstructing Duodenal Ulcer  
Gastro-enterostomy—Feb 23, 1940

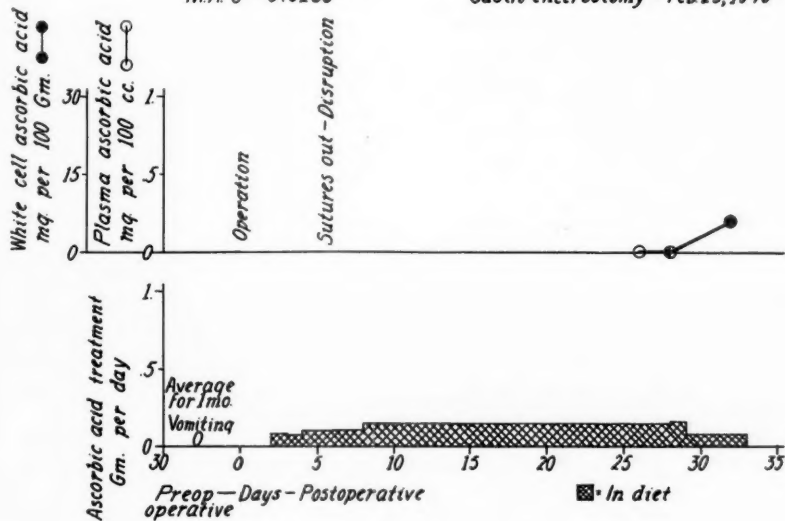
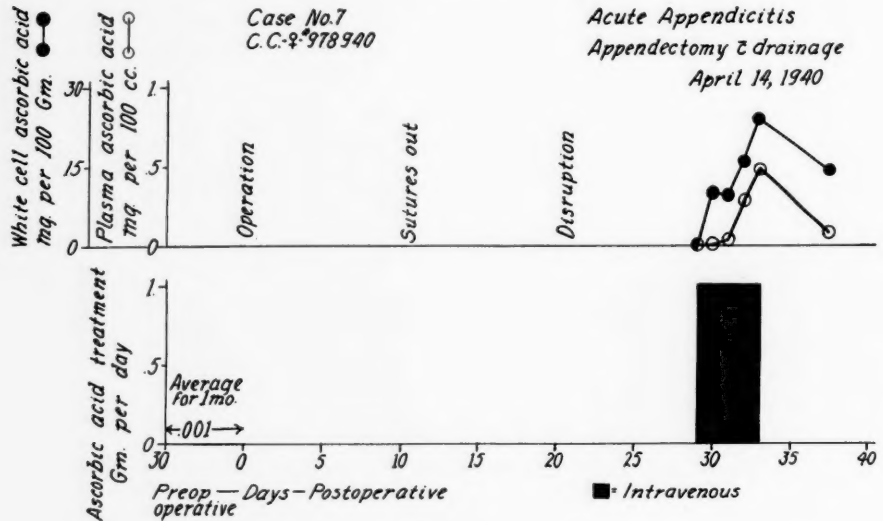


CHART 6.

did not have an opportunity to determine the blood levels until after 22 days of high orange juice diet. Even at this time the plasma and white blood cell levels were extremely low.

*Comment.*—This evidence points to a dangerous degree of scurvy. However, the removal of stay-sutures on the sixth day was inexcusable. The treatment of a man who vomits all his food should be by intravenous route.



**Case 7.**—*Near Scurvy.* Hosp. No. 978940: C. C., female, had acute appendicitis with peritonitis. Her diet before the illness had been very low in ascorbic acid containing foods. At operation, the appendix was removed, and the base of the cecum and the pelvis were drained. Stay-sutures were removed on the tenth day. The wound was moderately septic, and the patient was quite ill. Food was not taken well and no ascorbic acid given. On the twentieth day, a loop of intestine presented in the wound. This was replaced and held in by packing and strapping. Nine days later the patient was studied for scurvy and both the plasma and white cell levels were zero. The curve following the treatment proves a severe grade of deficiency.

*Comment.*—There can be little doubt that scurvy played a part in this late disruption.

**Case 8.**—*No Scurvy.* Hosp. No. 981871: C. B., male, had a subacute cholecystitis and a chronic gastric ulcer. His diet contained a small amount (about 12 mg. of vitamin C) before entering the hospital. At operation the gallbladder was drained. The stay-sutures were removed on the eighth day, and he promptly disrupted. His wound was resutured. Some days later, the first vitamin C determinations showed none in the plasma, but about 6 mg. per 100 Gm. in the leukocytes. After test doses the levels rose rapidly.

*Comment.*—This evidence indicates that scurvy was not present.

**Case 9.**—*No Scurvy.* Hosp. No. 986160: E. McN., male, young, had a traumatic rupture of the intestine, this time of the jejunum. His history showed a small intake of

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ascorbic acid before the injury. His stay-sutures were removed on the tenth day and he disrupted. He was resutured. Vitamin C determinations showed zero in the plasma and 12 mg. per 100 Gm. in the leukocytes. The test dose showed a rapid rise in both levels.

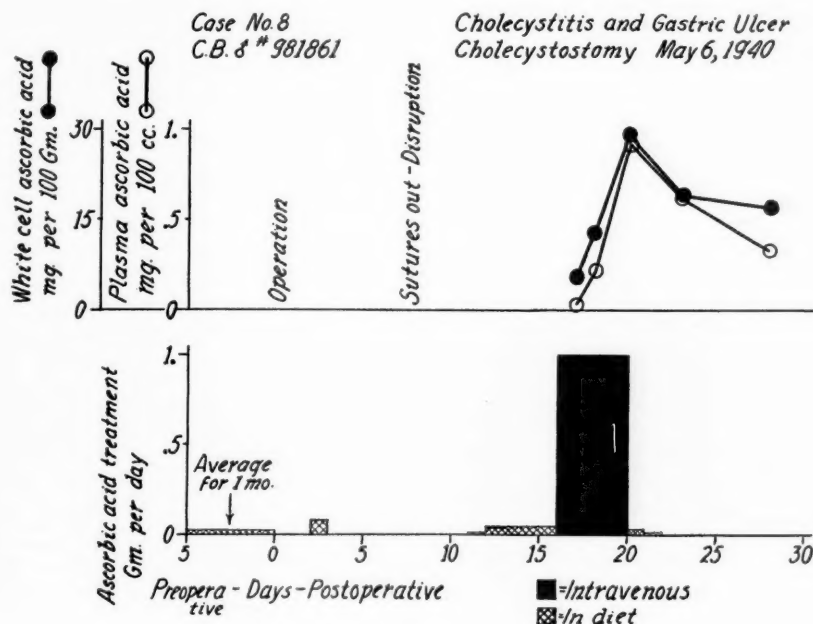


CHART 8.

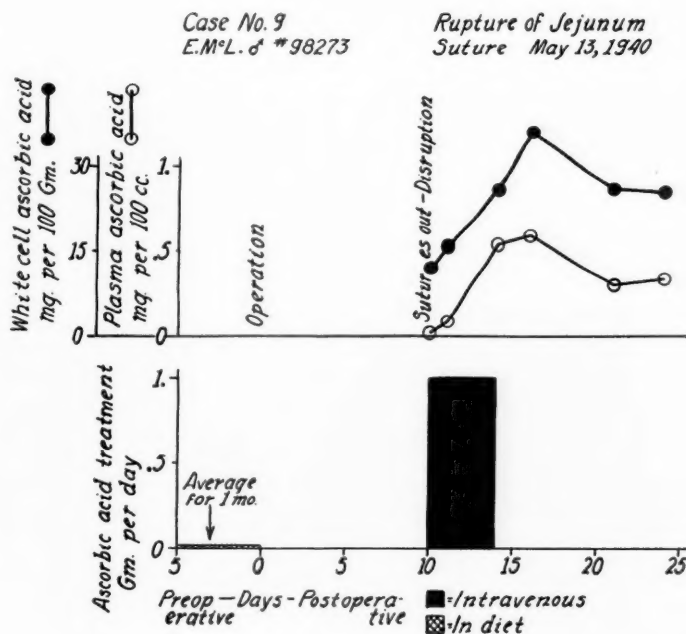


CHART 9.

*Comment.*—This finding, plus the response to test doses, proves the absence of scurvy.

**Case 10.**—*No Scurvy.* Hosp. No. 982674: J. M., male, had an obstructing duodenal ulcer. Although his preoperative leukocyte ascorbic acid was 14, he was given treatment intravenously with the results to the plasma and leukocyte levels shown on the chart. On the tenth day postoperatively the stay-sutures were removed and there was a small disruption. This was controlled by packing and strapping.

*Comment.*—Scurvy could have had no part in this accident.

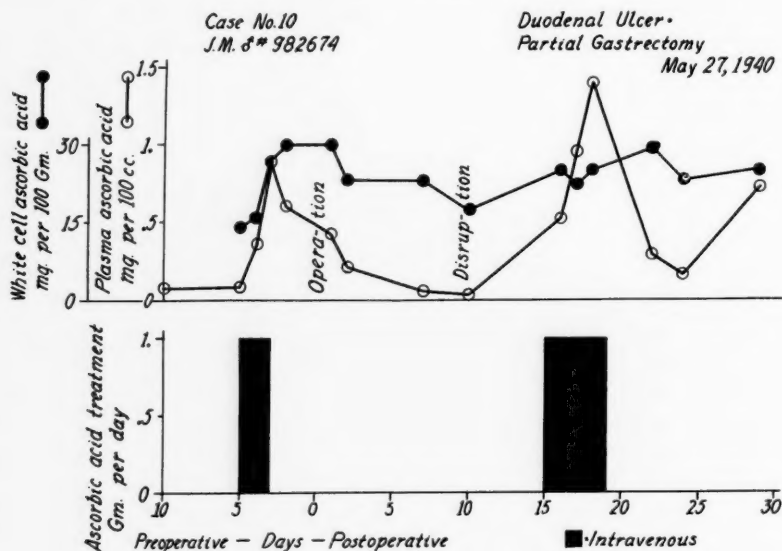


CHART 10.

**Case 11.**—*No Scurvy.* Hosp. No. 985945: P. B., male, rather feeble, with carcinoma of the sigmoid. He took a small amount of vitamin C in his food before operation. On the tenth day, his sutures were removed and he disrupted. His leukocyte level was eight. He was resutured and given vitamin C, but he died the next morning.

*Comment.*—With this leukocyte level the man could not have had a severe enough deficiency for it to be a factor in this disruption.

**Case 12.**—*No Scurvy.* Hosp. No. 995658: T. E. had a partial gastrectomy for duodenal ulcer. His preoperative diet had contained a small amount of vitamin C. On the sixth day, the stay-sutures were removed and the wound disrupted. It was resutured. The 0.5 Gm. doses of ascorbic acid were given for three days, after which the leukocyte level was 25 mg. per 100 Gm., and the plasma level 0.04 mg. per 100 cc.

*Comment.*—It is believed that the level of 25 mg. in the leukocytes, after only 1.5 Gm. of treatment, indicates that the wound was not affected by lack of vitamin C.

*Discussion.*—Twelve cases of disruption of abdominal wounds have been studied. Scurvy played no part in the accident in Cases 1, 3, 5, 8, 9, 10, 11, and 12. This statement is made in spite of the fact that most of these cases

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had very low plasma vitamin C levels, at one time or another, during their illness. Cases 2, 6, and 7, had a severe depletion of their vitamin C reserves, and scurvy probably delayed, or prevented, the healing of their wounds. (Case 4 is doubtful.)

In none of the cases was the method of suturing up to the standards of technic set up by Whipple. On the other hand, it must be stated that these disruptions occurred among a very large number of abdominal operations,

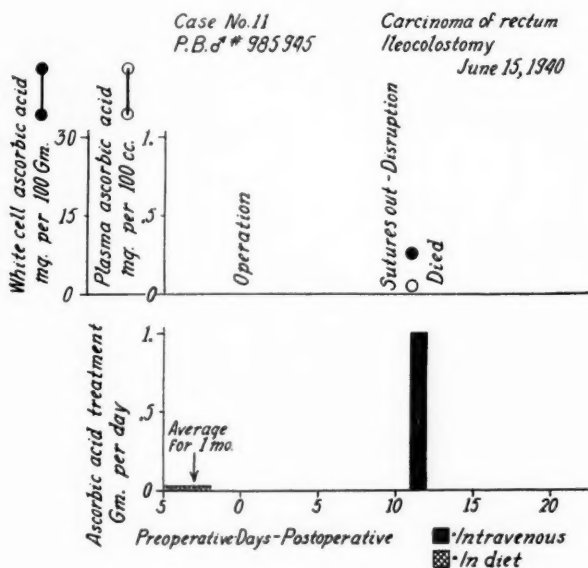


CHART 11.

and the percentage of these accidents is low, showing that the methods of suturing used were, at least, reasonably good. Stay-sutures were used in all cases, and in some cases were removed much too early. If stay-sutures are put in for a purpose, the purpose must be to support the wound until natural healing has taken place sufficiently to make their presence superfluous. This makes it imperative that they remain, at least, until the twelfth or the fourteenth day.

It is obvious from the cases presented that a larger part of the problem of disruption will be solved by improved technic than by studies of or treatment with vitamin C. On the other hand, the fact that a few cases of disruption occur in patients with severe depletion of the vitamin C reserves, indicates that these reserves should be studied before operation. A series of gastric and duodenal ulcer patients who were in the hospital at the same time as those cases reported here, are also being studied and will be reported in another communication. Several of them had deficiencies comparable to that of Case 7, above. However, their deficiencies were corrected either just before or just after operation. If they had not been treated, the number of



cases disrupting from ascorbic acid deficiency might have been larger. Most surgical services have no facilities for such studies and such studies are extremely expensive. The authors are convinced that wide installation of such facilities are not necessary at present. In another communication, we hope, shortly, to prove that a few minutes spent in securing and analyzing a short dietary history will do as much or more to determine these reserves than ascorbic acid determinations. In such a history, special attention should be given to the amounts of certain foods that are eaten per day. About

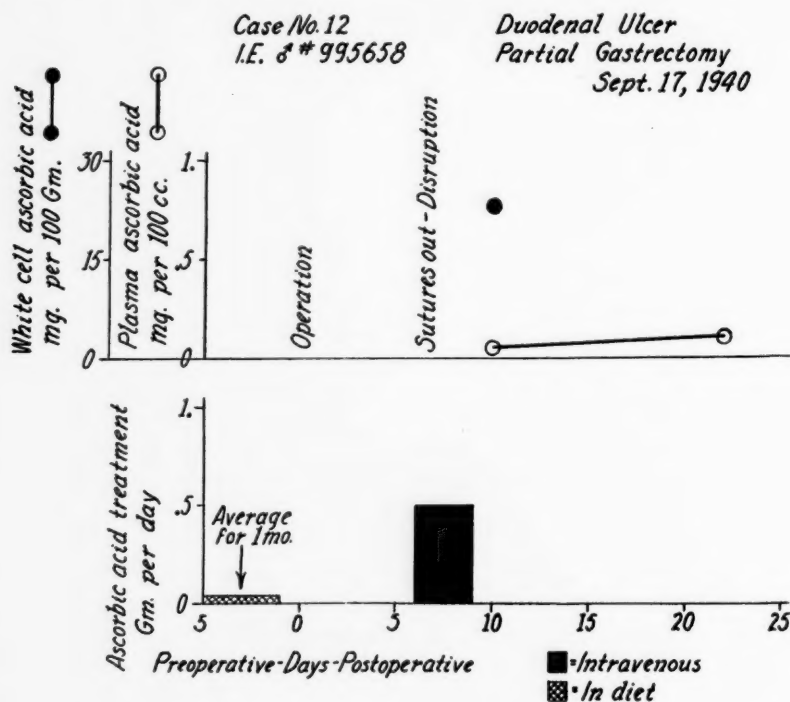


CHART 12.

75 mg. of ascorbic acid is generally accepted as an amount that will keep a well person saturated. We believe that even 20 mg. will keep sufficient reserves so that wounds will heal easily and well. Seventy-five mg. will be furnished by the amounts of food shown in Table II. Many other foods have

TABLE II

AMOUNTS OF CERTAIN FOODS NEEDED, DAILY, TO FURNISH 75 MG. OF ASCORBIC ACID,  
IF THE PARTICULAR FOOD IS THE ONLY SOURCE OF THE VITAMIN

Fresh citrus fruit or juice and fresh strawberries.....	150 Gm. or cc.
Canned citrus fruit.....	250 Gm. or cc.
Fresh or canned tomatoes or tomato juice.....	300 Gm. or cc.
Cooked liver.....	300 Gm.
Cooked potatoes (except fried).....	300 Gm.
Raw apples, pears, other fruits and berries.....	1-5 Kg.

Lettuce, other greens, and most vegetables contain small amounts, and part of these small amounts may survive cooking.

small amounts of this vitamin, but grains and flour have none, and pasteurized milk very little.

Full data of this nature has been presented by Daniel, and Munsell,<sup>21</sup> and by many other students of diet.

Following the securing of data from the diet, those patients with very low reserves should be treated. The treatment should be given preoperatively in an "elective" case, and immediately postoperatively in an "emergency" case. Ascorbic acid is cheap and may be given by mouth, intramuscularly or intravenously (using different preparations). About 4 Gm. are needed to bring a severe case of scurvy up to saturation. This may safely be given in four days. Be sure, however, that the treatment be intramuscular or intravenous if there is likely to be vomiting or diarrhea, otherwise it makes no difference which way it is given.

#### SUMMARY AND CONCLUSIONS

(1) A study of preoperative diet and preoperative plasma vitamin C levels of patients having operations upon the biliary tract was made.

(2) Those with poor intake or low levels or both, had a higher percentage of postoperative herniae than those with better intakes or levels.

(3) A study of 12 cases of abdominal wound disruption shows that mechanical factors were more frequently the determining ones for disruption than depletion of vitamin C reserves in this series.

(4) Three cases, however, had sufficient degrees of ascorbic acid deficiency, so that this was an important factor in their disruptions. In a fourth case, depletion to a dangerously low level may have taken place, but the data are too incomplete to be sure.

(5) Two cases of depleted reserves were associated with lesions of the stomach, and two (including the doubtful one) with appendicitis.

(6) These studies indicate a need for improvement in surgical technic, and for routine study of vitamin C reserves by surgeons.

(7) Study of vitamin C reserves may be made by means of dietary histories and should be followed by preoperative, or early postoperative treatment of the few patients that probably have low reserves.

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THE EFFECT OF THE LOCAL AND ORAL ADMINISTRATION OF  
COD LIVER OIL ON THE RATE OF WOUND HEALING IN  
VITAMIN A-DEFICIENT AND NORMAL RATS \*

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In a previous paper,<sup>1</sup> we reported that the topical application of cod liver oil healed ulcers of the lower extremity of diabetic patients more effectively than a controlled group who were not thus treated. In an effort to determine more accurately the effect of cod liver oil on the rate of healing of wounds, the following study was undertaken.

Cod liver oil has been used locally in the healing of wounds and burns in patients since 1934.<sup>2-7</sup> All observers report an increase in the rate of wound healing and a decrease in the severity of infection when present. Experimentally, Kemmler,<sup>7</sup> Proto,<sup>8</sup> and Löhr and Unger,<sup>9</sup> have studied the effects of cod liver oil upon rabbits and guinea-pigs, and have found it effective in accelerating wound healing. There are three factors in cod liver oil which might be responsible for its healing effect: These are vitamins A and D and the unsaturated fatty acids. Vitamin D is concerned principally with the metabolism of calcium, and, unless the wounds involved the bony structures, or the animals were on diets deficient in calcium or vitamin D, the effect on the healing of wounds involving epithelial structures would be slight, if any. Vitamin A, on the other hand, is known to affect the epithelial tissues, and a deficiency of this vitamin results in hyperkeratinization of the epithelium. The unsaturated fatty acids are concerned with the condition of the skin, and in animals deprived of linolic or linolenic acids<sup>10</sup> dryness and scaliness of the skin occurs.

In the present study, we are reporting the effects of cod liver oil and linseed oil, applied locally, on the rate of wound healing in rats. In addition, one group of vitamin A-deficient rats were fed an equivalent amount of cod liver oil to find out if the parenteral administration was as effective in healing the wounds as was the direct local application of the vitamin. Both normal and vitamin A-deficient rats were used in order to compare the rate of healing in entirely normal animals with the rate of healing in the deficient animals.

*Procedure.*—All the rats were bred in this laboratory from an original Wistar strain, and the experiments were made on litter mates.

The normal rats consisted of litters fed the laboratory stock diet of which the vitamin A content was 245 I.U. per 100 Gm. They were wounded at the same age as the vitamin A-deficient rats, which was the time at which

\* This data was included in a thesis by Dr. Harold Brandaleone for the Degree of Doctor of Medical Science in New York University, New York, N. Y.

the latter developed the signs of vitamin A deficiency, and was at an average age of 107 days. When wounded, the normal animals were divided into two groups, Group B—in which the wounds were allowed to heal without treatment of any kind; and Group D—in which the wounds were treated with cod liver oil.

The animals which were to be depleted of their vitamin A stores were started on the vitamin A-deficient diet when age 27 to 37 days. The diet consisted of casein 9.61 per cent, salt mixture 3.85 per cent, sodium chloride 0.96 per cent, dried brewer's yeast 9.61 per cent, cornstarch 56.75 per cent, Crisco 19.22 per cent, and 0.3 Gm. of viosterol was added to 1,000 Gm. of this mixture. The animals were allowed to eat the diet *ad lib.* When the symptoms of the deficiency began to occur, the rats were wounded. Four groups of animals were studied on the vitamin A-deficient diet: Group A—in which no local treatment of any kind was used on the wounds; Group C—in which cod liver oil was applied to the wounds; Group G—in which the wounds were treated with unboiled linseed oil, the iodine number of which was 158; and Group H—in which the wounds were not treated but the rats were fed the same amount of cod liver oil as was applied locally to the wounds of the animals in Group C (Table I).

TABLE I  
STATUS OF THE GROUPS OF RATS STUDIED

Group	No. of Rats	Mortality	Infection	Condition of Animals, and Treatment of Wounds
A (1 and 2)	62	60%	22%	Rats were fed diet deficient in vitamin A. Wounds were untreated. The diet of the parents of A <sub>1</sub> was higher in vitamin A than the diets of the parents of A <sub>2</sub>
C	52	0	0	Rats were fed diet deficient in vitamin A. Wounds were treated with cod liver oil
G	49	41%	10%	Rats fed diet deficient in vitamin A. Wounds were treated with unboiled linseed oil (iodine number 158)
H	29	0	0	Rats fed vitamin A-deficient diet. Wounds were untreated. Cod liver oil fed by mouth
B (1 and 2)	45	0	5%	Rats were normal. Wounds were untreated. B <sub>2</sub> rats were 19 days older at the time of wounding than rats in B <sub>1</sub> group
D	40	0	0	Rats were normal. Wounds were treated with cod liver oil

The animals on the vitamin A-deficient diets were wounded at the time when they failed to show any increase in weight for a period of seven days. This was before any other pronounced symptoms of vitamin A deficiency had appeared, for we found that, if wounding was delayed longer, the rats died soon after the wounds were made.

*Manner of Wounding and Method of Measuring Wounds.*—All the rats were wounded as follows: The hair over the thoracic vertebrae was clipped, the skin shaved clean and grasped with a pair of forceps, and an elliptical wound extending through subcutaneous tissues was made with a pair of scissors. An impression of the shape of each wound was taken by placing a piece of filter paper over the fresh wound. The wound was not measured



until the day after it was made, in order to obviate any error due to the stretching of the skin which occurred immediately after wounding. The long and wide diameters were measured in centimeters with calipers. Measurements were taken two or three times a week until the wound was completely healed, or the animal died. In the latter case, the diameter of the wound at the time of death was measured. The calculations of the total area in each wound was elliptical in shape. This formula is  $\frac{\pi}{4} \times a \times b = \frac{3.14}{4} \times a \times b = 0.785 \times a \times b$ . In order to prevent the animal from licking or scratching the wound, a metal cap approximately 2 cm. in height and 2.5 cm. in diameter was shaped to the back of the animal and attached with adhesive tape wrapped around the abdomen. The oils were dropped on the wound from a measured dropper. Enough oil was applied to just cover the wound; from two to four drops at first, and, as the wound became smaller, one drop. The amount of vitamin A was calculated from the total number of drops of cod liver oil used. Treatment with cod liver oil or linseed oil was begun 24 hours after wounding and was repeated daily.\*

At the end of the experiment, an average period of 20 days, the animals were anesthetized and exsanguinated. The wounded area was excised and preserved in 10 per cent formalin solution for histologic examination. The wound was considered healed when complete epithelium covered the wound and a white scar was present.

#### RESULTS ON THE RATE OF WOUND HEALING

##### (1) In the Vitamin A-Deficient Rats (Groups A, C, G, and H)

*Group A* (vitamin A-deficient rats whose wounds were *not treated* with any agent).—This group was subdivided into two parts ( $A_1$  and  $A_2$ ) because the parents of the rats in Group  $A_1$  were on a higher vitamin A diet than the parents of the rats in Group  $A_2$ . However, once the animals had become vitamin A-deficient the rate of wound healing was the same in all the animals. Group  $A_1$  healed at the rate of 0.046 sq. cm. daily; Group  $A_2$  at the rate of 0.045 sq. cm. daily. Calculated as a single group, the daily rate of healing was 0.045 sq. cm.  $\pm$  S.D.  $\dagger$  0.035 (Table II).

*Group C* (vitamin A-deficient rats whose wounds were *treated with cod liver oil*).—In this group the daily rate of healing was 0.088 sq. cm. with a standard deviation of  $\pm 0.027$ . This was significantly greater than in Group A, whose wounds were untreated.

The standard deviations were calculated from the formula<sup>11</sup>  $S.D. = \sqrt{\frac{d^2}{n-1}}$ . Comparing Groups A and C, the value for *E* is significant as shown in Table III.

\* The cod liver oil was supplied by the Mead-Johnson Laboratories. The vitamin A content of the cod liver oil was 668 international units per gram.

$\dagger$  S.D. = Standard deviation =  $\sqrt{\frac{d^2}{n-1}}$ .

*Group H* (vitamin A-deficient rats whose wounds were *untreated but who were fed cod liver oil*).—The average rate of healing in this group was 0.069 sq. cm.  $\pm$  S.D. 0.021. This rate of healing was significantly faster than in the untreated A-deficient rats but slower than in the wounds treated locally in the A-deficient rats.

TABLE II  
EFFECT OF COD LIVER OIL ON THE DAILY RATE OF  
WOUND HEALING IN NORMAL AND VITAMIN A-DEFICIENT RATS†

Group	No. of Rats	Condition of Rats	Daily Rate of Healing Sq. Cm. $\pm$ S.D.*	Total U.S.P. Units Contained in Cod Liver Oil Given	Weight Change from the Time of Wounding to Death
A	45	Vitamin A-deficient. No cod liver oil	0.045 $\pm$ 0.035	None	-27 Gm.
C	38	Vitamin A-deficient. Treated locally with cod liver oil	0.088 $\pm$ 0.027	483	+16 Gm.
G	37	Vitamin A-deficient. Treated locally with linseed oil	0.051 $\pm$ 0.043	None†	-35 Gm.
H	19	Vitamin A-deficient. Fed cod liver oil. No local treatment to wound	0.069 $\pm$ 0.021	358	+34 Gm.
B	39	Normal rats. No cod liver oil applied locally	0.082 $\pm$ 0.025	None	+32 Gm.
D	35	Normal rats. Treated with cod liver oil locally	0.087 $\pm$ 0.028	645	+ 6 Gm.

\* S.D. = Standard deviation =  $\sqrt{\frac{d^2}{n-1}}$ .

† Wounds treated with a total of 1.196 Gm. of unboiled linseed oil.

‡ This table includes all wounds whether completely or partially healed.

*Group G* (vitamin A-deficient rats whose wounds were *treated with linseed oil*).—In this group the daily rate of healing was 0.051 sq. cm.  $\pm$  S.D. 0.043. This is not significantly different from Group A but is significantly different from Group C. The results with linseed oil indicate that these unsaturated fatty acids do not exert a healing effect.

## (2) The Rate of Wound Healing in the Normal Rats (Groups B and D)

Both of these groups were absolutely normal rats, on entirely adequate diets. There was practically no difference in the rate of wound healing between Group B whose wounds were not treated with cod liver oil, and Group D, whose wounds were treated. The average daily rate of healing in Group B was 0.082  $\pm$  S.D. 0.025; and in Group D 0.087  $\pm$  S.D. 0.028 (Table II). Apparently, cod liver oil, applied locally to this type of wound in well-nourished normal rats, does not significantly affect the rate of wound healing.

The statistical comparisons of the rate of wound healing between the various groups is given in Table III. The differences between Groups A and C, C and G, C and H, A and H, and B and H are significant. According to Chaddock,<sup>11</sup> for the differences to be significant the value of E should be

TABLE III

COMPARISON OF VARIOUS GROUPS OF RATS WITH RESPECT TO DAILY RATE OF WOUND HEALING

Groups Compared	Difference between the Means (Sq. Cm./Day)	Probable Error of the Difference between the Means	E* = Difference Between Means—Probable Error of the Difference between the Means
A and C	0.043	0.0047	9.1
B and C	0.006	0.0041	1.5
B and D	0.005	0.0045	1.1
C and D	0.001	0.0048	0.2
A and G	0.006	0.0059	1.0
C and G	0.037	0.0056	6.6
C and H	0.019	0.0043	4.4
A and H	0.024	0.0047	5.1
B and H	0.013	0.0042	3.1

\* E was calculated as the quotient of the difference between the means, divided by the probable error of the difference. The validity of this measure is supported by the fact that the plotted data approximate a normal distribution curve.

above 2.5. Groups B, C and D are not statistically different. The rate of wound healing in the vitamin A-deficient rats treated with cod liver oil was approximately the same as the rate of wound healing in the two normal groups.

### (3) *Observations on the General Condition of the Animals in the Different Groups*

In the vitamin A-deficient groups, A and G, receiving no cod liver oil locally, the symptoms of vitamin deficiency persisted after wounding. These symptoms included loss of weight, fur changes, anorexia, humpback, crusting of the nose and eyes, and xerophthalmia. The average loss of weight in these two groups was 32 Gm. during the period of observation. In Group C, where the wounds were treated with cod liver oil, there was an average gain of 16 Gm. during the experimental period. Although the symptoms of vitamin A deficiency persisted in some of the animals, they were much less severe and less frequent. This was not due to licking the oil off the wounds, as the metal caps placed on the wounds prevented the animal from reaching the wound with his paws or tongue. In the vitamin A-deficient rats fed cod liver oil (Group H) the symptoms of vitamin A deficiency were rapidly controlled, and these animals gained an average of 34 Gm. during the period of observation. None of the animals died, and no infections occurred in the group.

In Group A, the wounds healed completely in only 18 of the 45 rats; the other rats died before healing was effected. Of the 18 wounds healed, four showed possible evidence of infection (*i.e.*, pus and necrosis); of the 27 wounds that healed partially, six showed gross evidence of infection. In Group H, all of the wounds healed completely. In Group B, all the wounds healed completely, and there was gross evidence of infection in two of them. In Group G, of 37 wounds, 22 healed completely and six showed gross evidence of infection.

In the wounds treated with cod liver oil, the edges were even, in contrast

to the irregular edges in the untreated wounds; profuse granulation tissue was evident; and epithelization occurred earlier than in the untreated group, and was more abundant. The wounds finally closed leaving a small, white scar.

*Discussion.*—The absorption of certain vitamins through the skin has been established.<sup>15</sup> Helmer and Jansen<sup>16</sup> demonstrated that vitamin A, contained in halibut liver oil and carotene, is readily absorbed through the skin of rats, preventing the severe symptoms of vitamin A deficiency. Eddy and Howell<sup>17</sup> demonstrated the absorption of vitamin A through the unbroken skin of rats. Judging from our results, the local application of cod liver oil to the wounds of vitamin A-deficient rats will increase the daily rate of healing and will improve the general nutritional state of the animals. The feeding of cod liver oil is not as effective in healing wounds as is the local application.

Just what factor in cod liver oil is responsible for the healing effect remains to be determined. Apparently, it is not the unsaturated fatty acids, as linseed oil contains large amounts of the unsaturated fatty acids, with the exception of arachidonic acid. Getz,<sup>12</sup> working on tuberculous ulcers in guinea-pigs, has shown that the healing agent in cod liver oil is contained in the "vitamin fraction." He also reports that more rapid healing did not occur when fish oils with higher concentrations of vitamins A and D were used. If vitamins A and D were the only factors responsible, one might expect that the rapidity of the healing process would parallel the increased concentration of the vitamins. As there is, undoubtedly, a limit to the rapidity with which healing can occur, and, as this may have been reached at the lower concentration of the vitamins, such a correlation between the rate of healing and the concentration of the vitamins may not hold. The majority of investigators agree with Getz that the unsaponifiable or "vitamin fraction" of cod liver oil contains the healing agent. Up to the present time, no other single factor has been isolated.

In our *normal* animals, the local application of cod liver oil had no significant effect on the rate of healing. There might seem to be some discrepancy in this respect between our results and those of other observers, who report beneficial effects from the application of cod liver oil to burns,<sup>13</sup> and in tuberculous lesions in normal animals,<sup>14</sup> and in crushing wounds and burns in animals.<sup>2a</sup> In this study, the normal animals were in an optimal state of nutrition, and the wounds were made with as little trauma as possible, so that there was no injury to the deep tissues. The types of wounds in which cod liver oil has been effective in patients have been traumatic; *e.g.*, crushing wounds or burns, or wounds secondary to a metabolic disorder,<sup>1, 2, 3, 4, 6, 8</sup> and the nutritional status of the patients probably was not optimal. In these normals, the rate of healing that occurred represents the normal rate, and as far as we know at the present time, the maximum rate of healing. It may be that this rate of healing can be further increased by some more potent agent but, obviously, a point will be reached at which no further increase in the rate of healing can occur.

Drigalski<sup>14</sup> found that cod liver oil had a definite bacteriostatic as well as bactericidal action, and believes that it tends to hinder the passage of toxins from wounds into adjacent tissue. In our series, no infections occurred in the wounds in either the normal or vitamin A-deficient animals treated with cod liver oil or fed with it. No special precautions were taken in any of the animals to avoid infection. In the normal animals whose wounds were not treated with cod liver oil, there was evidence of infection in two of them. The incidence of infection in the vitamin A-deficient untreated groups was quite definite, averaging 20 per cent. Sixty per cent of the animals in this group died before complete healing had occurred.

It is particularly interesting to note that the local application of cod liver oil was more effective in increasing the daily rate of healing than was the feeding of cod liver oil. The effect of the local application, apparently, is a direct as well as a general one, as the nutritional state of these animals was also improved.

Calculation of the total number of days required for complete healing of wounds in the various groups could not be satisfactorily evaluated. First, because in the A-deficient group some of the animals died before complete healing occurred. Secondly, the exact end-point of healing could not be determined to the hour at which it occurred, and it was, therefore, difficult to calculate the total number of days and hours required for complete healing. Obviously, a time interval of 24 hours becomes too large a unit for the accurate estimation of the healing of wounds of small dimensions.

#### CONCLUSIONS

(1) The daily rate of healing in experimentally wounded vitamin A-deficient rats was accelerated by the direct application of cod liver oil to the wounds. The direct application of cod liver oil did not increase the daily rate of wound healing in normal rats.

(2) Linseed oil, directly applied to the wounds, did not significantly increase the daily rate of healing in vitamin A-deficient rats.

(3) The feeding of cod liver oil increased the daily rate of healing in the vitamin A-deficient rats but not to as great a degree as did the local application of cod liver oil.

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# BRIEF COMMUNICATION

## TABLE TOP FOR ROENTGENOGRAPHY, ESPECIALLY OF THE BILIARY TRACT, DURING OPERATION

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ROENTGENOGRAPHY during operation has found certain limited applications, as for example in bone operations, search for foreign body, exploration of biliary ducts, and combined instrumental and roentgenographic examination of the uterine cavity. When its technic has been simplified, as in examination of the exposed kidney, it has become popular. But cumbersomeness of method has retarded most of its potential uses. Sliding a cassette either directly beneath the patient or into a "tunnel" opening at the side of the

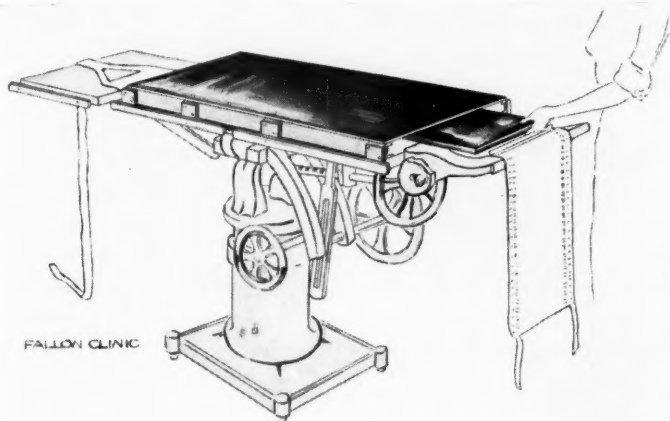


FIG. 1.—Roentgenographic overtop. The cassette is maneuvered from the ends of the table without disturbing the operation.

operating table disrupts the sequence of the operation, distracts the operating team and jeopardizes sterility. But a space beneath the patient, opening at the ends rather than at the side of the table, would allow manipulating the cassette without disturbing patient, drapes or team.

Such an end-opening space is provided by an overtop\* made of one-eighth-inch (3 Mm.) "Masonite," a wood composition chosen as the least radiopaque of several materials tested, resting upon metal side walls which lock into the side-rails of the table. It replaces those sections of the cushion

\* Manufactured by the Scanlan-Morris Co., Madison, Wis.

under the torso. Beneath the overtop, on the top of the table, slides a wide canvas belt with a frame to hold the cassette. One end of this belt leads over the head of the table and from the other a strap leads to its foot. By these the cassette may be pulled either sidewise or to-and-fro by the roentgenologist and anesthetist, standing at opposite ends of the table, and well away from the operating area. Inserting a fresh cassette involves only lifting the patient's head. A yardstick held beside the patient shows how far from the end of the table the cassette should be, and an inch scale printed on the belt shows how far from the end it is. A large film (14x17 inches, 35x43 cm.) gives latitude in aiming the rays. A Lysholm grid substitutes for a Bucky. The grid is light and thin, moves with the cassette and obviates a mechanism for tripping a Bucky.

To permit holding the breath, spinal anesthesia is advisable for some roentgenograms, especially cholangiograms. Ordinarily, the operator covers the patient with a large sterile sheet on which he marks the center of the field with a dab of blood, then steps back to give place for the portable roentgen unit, while the assistants hold their retraction.

In calculating exposure, therefore, the roentgenologist must allow for the tissues retracted out of the path of the rays. Exposure factors for a cholangiogram with brominized oil are: 75-88 Kv., ten Ma., 17 inch (43 cm.) distance, one second, cone five inches (13 cm.) in diameter and six inches (15 cm.) long, superspeed intensifying screen. If a Lysholm grid is used—we usually have found it unnecessary—the exposure is three seconds. Film development time may be cut to a minute by quick developers, such as a modification of their D-8 formula obtainable from the Eastman Kodak Co.

Four years' use of this apparatus has disclosed two disadvantages. The thin top sags beneath extremely heavy patients. But we nevertheless prefer it to a thicker top, because these are just the patients who need the least possible added opacity. Secondly, the absence of a cushion increases the incidence of postoperative backache, so the apparatus should not be used routinely but only when it is likely to help.

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Figures 9 and 10 in the article on "Surgical Problems of War," by Mr. L. R. Broster, in the June, 1941, ANNALS OF SURGERY, in addition to the acknowledgment to the Royal Society of Medicine should have carried credit to Dr. E. G. L. Bywaters and Dr. D. Beall.

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